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THE MEDICAL CLINICS
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VOLUME 4 NUMBER 4

CLINIC OF DR. ALFRED STENGEL

UNIVERSITY HOSPITAL[1]

## ON THE USE OF SERUM AND BLOOD OF CONVALESCENT PATIENTS IN THE TREATMENT OF LOBAR PNEUMONIA AND INFLUENZAL PNEUMONIA

I WISH to present today 2 cases of lobar pneumonia, one showing spontaneous recovery, the second an immediate crisis and beginning convalescence on the fifth day of the disease following intravenous injection of blood-serum from the first case, and will follow with a report of our previous experience in other cases.

**Serum Donor, Case A.**—Mr. H. B., aged twenty-one, student, after a severe exposure developed a "heavy cold in his chest" on December 12th, but though chilly and feeling ill continued up and about until December 14th, when he had more pronounced chills and vomited. His fever rose sharply after the chill. Severe pleuritic pain in the lower left chest and painful coughing with blood-stained expectoration followed. On admission to the hospital, the same day, clear signs of consolidation of the left lower lobe were detected, and his leukocytes numbered 23,200, the neutrophils being 85 per cent. The sputum was found to contain Type II pneumococci.

Strapping gave great relief to the pleuritic pain. The rest of his treatment consisted of moderate doses of quinin (1 gm. daily) and tincture of digitalis with solution of potassium citrate. After twenty-four hours of continuous fever at about 103° F.,

[1] December 21, 1920.

the temperature fell rapidly to about 101° F., then a gradual decline occupied the next three days, the normal being reached on the eighth day after the first symptoms.

On December 19th, after the crisis and return to normal temperature, 225 c.c. of blood were taken from his median basilic vein and allowed to coagulate on ice. The serum was centrifugated to clear it of suspended matters. Culture of the serum

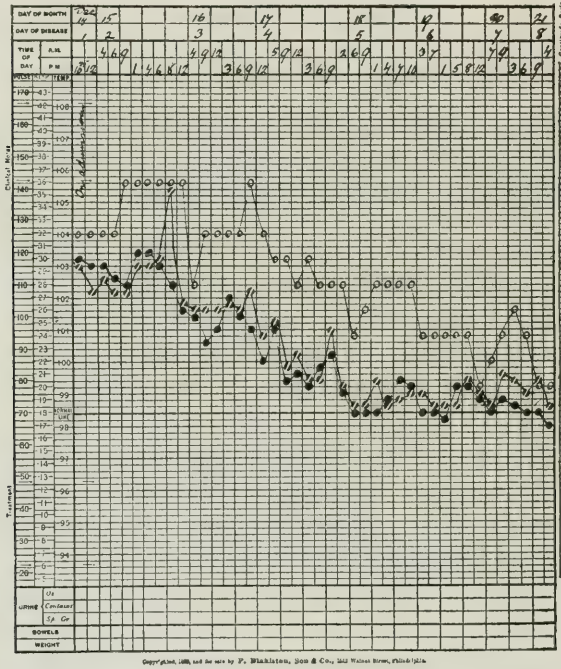

Fig. 91.—Serum donor, Case A, bled for serum December 19th.

was made and reported "no growth" on December 20th. The patient had a slight reactive rise of temperature (99° F.) after the withdrawal of blood, but this subsided in a few hours and convalescence proceeded rapidly.

**Case I.**—Mr. R. S., aged nineteen, a student, was admitted on December 17th. He had had a "cold" for about a week, but did not feel particularly ill. On December 16th severe headache,

weakness, and vomiting set in, and increase of cough with blood-tinged expectoration occurred at the same time.

At the age of six years he had an attack of acute articular rheumatism, and several lesser attacks followed in the next five years, but his heart was not recognizably affected.

On physical examination at admission to the hospital distinct consolidation of the left lower lobe was found. The breathing

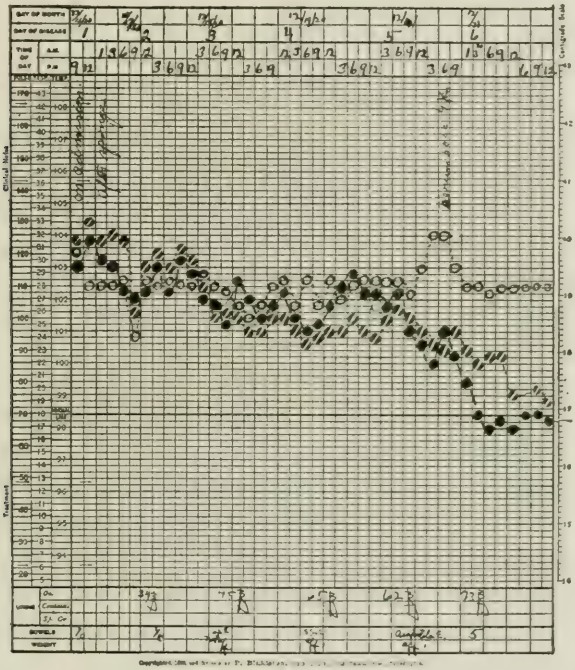

Fig. 92.—Case I. Serum (50 c.c.) from Case A intravenously on fifth day.

was tubular, and without râles. A systolic murmur was heard at the apex of the heart and the left border of the heart was displaced slightly to the left. Leukocytes 35,800; neutrophils 89 per cent.

The patient's general condition was more unsatisfactory than appears from the chart. The dyspnea was not a pronounced symptom, but frequent coughing with blood-tinged expectoration, incessant vomiting, and prostration of strength were marked.

On December 20th (fifth day of disease) there was some decline of fever, but it had risen again, and the chest signs seemed increasing rather than diminishing. At 4.30 P. M. 50 c.c. of serum from Case A were administered intravenously. The immediate crisis following the injection is well shown in the accompanying chart. No reaction of any kind followed the injection and the crisis was unattended by any pronounced symptoms.

*Later Notes.*—Physical examination (December 21st) showed marked improvement in the degree of dulness and the character of the breath sounds, but there were few râles. On December 22d at 10 A. M. the signs at the left base had largely vanished. The continuance of the same rate of respirations after critical decline of temperature and pulse-rate has been the principal feature of interest. The disturbance of stomach (vomiting) continued up to the time of crisis and then quickly subsided.

Both cases were reported to us as Type II infections. In the series of lobar pneumonias we treated in 1916–17, which will be detailed presently, I am unable to report on the type in all cases treated or for the donors of the serum, and I have no definite opinion to offer from our observations as to the particular advantage derivable from the use of serum derived from a case of a certain type in corresponding types of the disease. After our preliminary experiences with this method of treatment we hoped to investigate the special advantage of serum from one type in the same type of infection, but a lack of sufficient clinical material and other difficulties prevented our following up this problem.

The striking result seen in this case (Case I) was seen in a considerable proportion of the cases included in the two series of cases to which I shall presently call your attention. In some patients the beneficial effects following serum injections were little short of dramatic; in some though not as strikingly rapid results followed, no doubt could be entertained regarding the improvement in the patient's condition; in a few cases gradual amelioration of the symptoms with slow decline of temperature occurred.

In your studies regarding the treatment of pneumonia you

have learned that the treatment of this disease still remains highly unsatisfactory notwithstanding the fact that considerable advances seem to have been made in the direction of the production of specific sera for the treatment of certain types of cases. It is not my intention to discuss this aspect of the question today; suffice it to say that, so far as our present knowledge is concerned, considerable value seems to attach to the alien serum prepared for the treatment of cases of pneumonia due to the pneumococcus of Type I, but little has been accomplished in the direction of controlling or curing cases caused by other types of pneumococci.

You are, of course, familiar with the fact that the typing of organisms offers some difficulties, and that unless the Type I serum is used in a routine manner until reports regarding the specific type concerned have been received much practical difficulty stands in the way of the general adoption of this method of treatment. So far as other types of pneumonia are concerned we are left without a specific form of management.

I may perhaps without hesitation add that certain forms of drug treatment apparently exercise some influence in the control of this disease, and much is yet to be learned regarding further possible advances in this direction. For many years quinin administered freely during the first few days of the disease has been regarded as having distinct curative value, and forms of quinin compounds carrying a high proportion of quinin have been recommended, though at the present time these special preparations are perhaps of less practical value in the treatment of pneumonia than the older and more familiar salts of the drug. Other treatment of the disease is mainly supportive and symptomatic. The special matter, however, that I wish to discuss today is the use of human serum obtained from convalescent patients, and I shall, therefore, omit any further reference to other forms of treatment.

Though the presence of immune bodies in the blood of convalescent cases of pneumonia was long ago recognized, and though some attempts at this plan of treatment were made in the early 90's, no practical results were achieved, and our

investigations were taken up during 1916–17 without much regard to previous investigations and, indeed, without any recollection of their existence.

When one considers the clinical history of the disease and studies the fever curve in pneumonia the suggestion readily offers itself that there must be a rapid liberation of some sort of antibodies at the time of the crisis to explain the rapid subsidence of the fever and the remarkable improvement in the general condition of the patient, particularly in the respiratory and the circulatory embarrassment that characterize the disease just prior to the crisis. It has often been asserted by therapeutic writers that the circulatory weakness and cardiac embarrassment in the late stages of pneumonia are due to the extent of the pulmonary consolidation and the consequent obstruction to the pulmonary circulation, and that the respiratory difficulties are similarly produced. When one observes, however, that immediately following the crisis the cardiac action is rapidly restored, pulse-rate diminished, and the respirations, previously rapid, shallow, and inadequate, assume more normal characters, while at the same time no change whatever is discoverable in the degree of consolidation or in the other physical signs, the thought is suggested that mechanical explanations will not suffice. It is apparently clear that the circulatory and repiratory embarrassments are toxic (centric) in origin and that their prompt relief at the time of the crisis is due to the removal or neutralization of toxic substances by antibodies. That such antibodies do develop in the blood as the result of pneumococcus infections was demonstrated many years ago by George and Felix Klemperer (Berlin. Klin. Woch., vol. xxviii, pp. 833–869), who found in the blood of rabbits immunized with pneumococci antibodies which were capable of exercising a protective influence in cases of experimental inoculation.

Subsequently Carter and Hughes (Therapeutic Gazette, October, 1892) used defibrinated blood from a convalescent pneumonia case in the treatment of a case of pneumonia, but obtained unsatisfactory results. Later Hughes (Transactions Pan-American Congress, 1893, p. 324) reported before the Pan-

American Congress a series of 13 cases in which convalescent serum was used for the treatment of pneumonia, but expressed distinct disappointment at the results he was able to observe. The serum was obtained by applying blisters, and is stated to have been taken from patients "never more than two weeks after convalescence and in many of them at an earlier date." A study of the case histories in this series indicates that the material was unpromising for any form of treatment, and it may also be noted that the method of obtaining serum was not a satisfactory one. The dosage of serum also was distinctly inadequate.

Andreoud (Revue de la Suisse Roman., February 20, 1893) records 3 cases in which small subcutaneous injections of whole blood from convalescent cases were employed. Only 2 or 3 c.c. of blood were used, and in but 1 of the cases was any result obtained that was at all definite.

After these early attempts no further practical steps were taken in the direction of the utilization of blood or serum from convalescent patients in the treatment of the disease.

Dochez (Studies from the Rockefeller Institute, vol. xvii, 1913, p. 506) reviews the literature bearing on the development of antibodies in the blood of experimental and spontaneous pneumococcus infections and reports regarding investigations of his own. He cites the work of the Klemperer brothers already mentioned, and the subsequent work of Neufeld and Handel, who demonstrated the presence of antibodies in the blood of mice and rabbits; also those of Strouse, whose results were not uniform, and Seligman and Klopstock, who failed entirely. In his own investigations postcritical serum was mixed with cultures of virulent organisms and the mixture injected into white mice. The serum from 14 cases of pneumonia was thus tested—in 10 against homologous organisms, in 3 against stock organisms, and in 1 against the organisms from a definite case. The protection was found more evident when the test was made with homologous organisms, and in all of the 10 cases in this series some effect was observable. In the 3 cases tested against stock organisms no effect was observed, while in the case tested against the organism from a definite case of pneumonia protection against 100

lethal doses of the organism was obtained. In one test of serum with two organisms—stock culture and a homologous culture—no protection was found against the stock culture, while the protection against the homologous culture was manifest up to one thousand times the lethal dose.

Regarding the time of appearance of antibodies in the blood Dochez states that in only 4 cases was any protective power demonstrable before the crisis. In 2 little or no power was found immediately after defervescence, but antibodies appeared at a later date—in 1 sixteen days after defervescence. In 7 patients the protective power was undiminished as long as the patients were under observation (five to twenty days), while in 5 cases diminution of the protective power was evident, amounting to a slight up to a complete loss of power. In several instances a slight return of protective power was noted late in convalescence, and in a few disappearance of the protective bodies occurred with slight return of fever, while in others the disappearance occurred during a totally afebrile convalescence. He concludes that the appearance of protective bodies coincides with the crisis of the disease. It may be noted that the method of investigation employed was one that might demonstrate the presence of antibodies capable of restraining the action of pneumococci or of destroying these organisms, but might have little or no value in showing the presence of other types of bodies that may be especially concerned in the processes involved in the crisis of the disease.

Without any special reference to Dochez's investigations, it had occurred to us that the phenomena of the crisis and the subsequent behavior of many cases of pneumonia justify the suspicion that antibodies are probably present in the circulation in greatest abundance at and imediately following the time of the crisis, and that in many cases these protective substances perhaps disappear shortly thereafter. As a probable proof of this assumpton it may be recalled that pleurisies and empyema of pneumococcic character frequently occur some days after sharp crises, and the assumption is perhaps not unwarranted that the occurrence of these complications is evidence that whatever

protective power may have been exercised during the crisis has been dissipated before the time of development of the complications named. Dochez's investigations seem to bear out this thought. At least his discovery that in some instances disappearance of the antibodies coincides with febrile recurrences seems to be proof in this direction.

Acting upon the assumption that antibodies may be present in greatest abundance just following the crisis, we undertook the treatment of a series of cases of pneumonia during the winter of 1916–17 by withdrawing blood from patients as soon after the crisis as possible and using the serum or in some cases the whole blood for the treatment of other cases. At the time named our typing of pneumonia cases was not as satisfactory as at present, and consequently it is impossible to state what results were obtained in particular types of cases, or the effect of blood or serum derived from particular types of cases.

Let me now give you briefly the outlines of the clinical histories of the cases in point.

### 1916–17 SERIES OF LOBAR PNEUMONIA CASES

**Case II.**—File No. 10,568. L. G. Age twenty-seven years. Admitted 9/10/16. Had had a "cold" for a week previously. The day before admission had sharp pain in left chest with repeated severe chills; deep breathing aggravated pain. Yellowish-red expectoration.

Physical examination showed pneumonia of the left base. Blood: 26,900 leukocytes, 91 per cent. neutrophils. Sputum rusty, contained pneumococci, Gram-negative rods, no tubercle bacilli.

9/13/16: At 12 noon (fifth day of disease) received intravenous injection of 15 c.c. of serum from a patient who had just passed the crisis of pneumonia. At 1 P. M. leukocytes 17,800; 3.55 P. M. 30 c.c. of serum from same patient injected intravenously; temperature 102° F.

9/14/16: At 9 A. M. temperature 99.1° F., leukocytes 12,800.

9/15/16: At 10 A. M. leukocytes 12,900, neutrophils 78 per

cent., temperature 100° F. At 1.15 P. M. 15 c.c. serum injected intravenously. At 3 P. M. and 6 P. M. temperature 99° F.

Subsequently temperature remained below 99° F. Resolution and convalesence rapid.

9/18/16: 175 c.c. of blood removed for collection of serum. Temperature at this time normal.

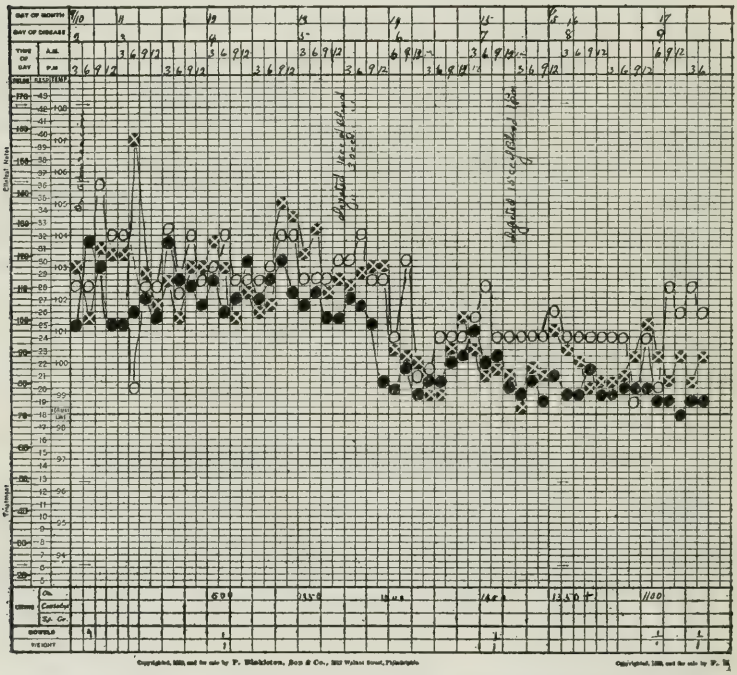

Fig. 93.—Case II. Lobar pneumonia. Serum (45 c.c.) on fifth day and 15 c.c. on seventh day.

**Case III.**—File No. 10,623. W. McG. Age thirty-nine years. Admitted 12/13/16. Patient, a poorly developed and alcoholic subject, was exposed to cold four days previously and developed chilly sensations later in the day. One severe chill during the night, delirious, and referred to the hospital.

Physical examination showed limitation of expansion and evidences of consolidation in the right upper and lower lobe with marked frictions in the axilla. Heart regular, no murmurs,

no enlargement. Temperature from 100° to 102° F. Blood: 22,400 leukocytes, neutrophils 89 per cent.

12/15/16: Some evidence of impairment of the left lung; heart distinctly weak. Patient's general condition very unsatisfactory; marked delirium.

12/16/16 (ninth day): 10 c.c. of serum injected intravenously.

12/17/16: Not much change.

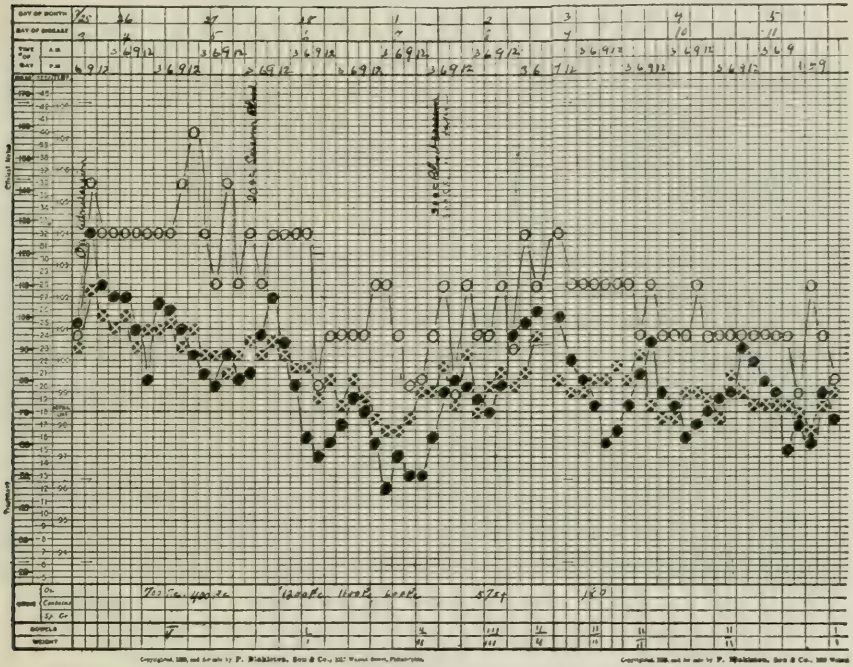

Fig. 94.—Case IV. Lobar pneumonia. Serum (20 c.c.) intramuscularly on fifth day.

12/18/16: Temperature falling gradually.

12/19/16: Temperature reached 99° F. Chest full of moist râles, especially at right base, but involving both sides.

12/20/16: Patient weaker and delirious.

12/21/16: Patient died, apparently of cardiac failure.

**Case IV.**—File No. 10,868. J. A. Aged sixty-three years. Admitted 2/25/17. Illness began 2/13/17 with pains in head, shoulders, and back, weakness and sweating.

2/20/17: Pain in the right side on deep breathing.

2/23/17: Severe chill and sweating; not much sputum.

Physical examination showed some jaundice, marked sclerosis of the vessels; Argyle-Robertson pupil; consolidation of the left upper lobe; distinct bronchial breathing. Temperature 101° to 103° F. Blood, 18,450 W. B. C.; neutrophils 86 per cent. Wassermann strongly positive. Urine, 1.017, dark amber, cloud of albumin, many brownish granular casts, bilirubin++.

2/27/17: Definite consolidation, crepitant râles, tubular breathing involving left upper lobe.

On the same day (four days after chill) 20 c.c. of serum injected intramuscularly at 2 P. M., temperature rose two degrees during the next six hours, and then rapidly fell to 97° F. during the night.

3/1/17: Signs clearing, but still present; 300 c.c. of blood removed for collection of serum (Wassermann report not yet received—serum discarded later).

Temperature rose to 101° F. on 3/2/17 and 100°+F. on 3/4/17 and 3/5/17, but was subnormal between the elevations. Subsequent convalescence uninterrupted.

**Case V.**—File No. 10,996. S. D. Aged twenty-five years, negro. Admitted 3/17/17. After being chilled three weeks previously, had several days of "cold" with fever; recovery apparently not complete.

3/16/16: Tried to resume his work, but fainted in the subway. Marked pain in chest on breathing. Temperature high.

Physical examination on admission: Marked signs of pneumonia at left base, scattered râles elsewhere, and on right side. Some friction at left base. Blood examination showed 19,900 leukocytes, 81 per cent. neutrophils. Sputum characteristic—pneumococcus Type I. Temperature continuous from 103° to 104° F. from admission 3/17 to 3/21.

3/20/17: Physical signs indicate increasing involvement of left upper lobe and marked râles in the left lower lobe, suggesting possibly beginning resolution.

3/21/17: Left base, marked consolidation, less suggestion of râles of resolution. Upper lobe definitely consolidated. At

12 M. (tenth day ?) 10 c.c. of serum injected intravenously. Temperature remained stationary until 9 P. M. 3/22, then rapid crisis and subsequent uninterrupted resolution.

3/26/17: Leukocytes 10,900, neutrophils 75 per cent.

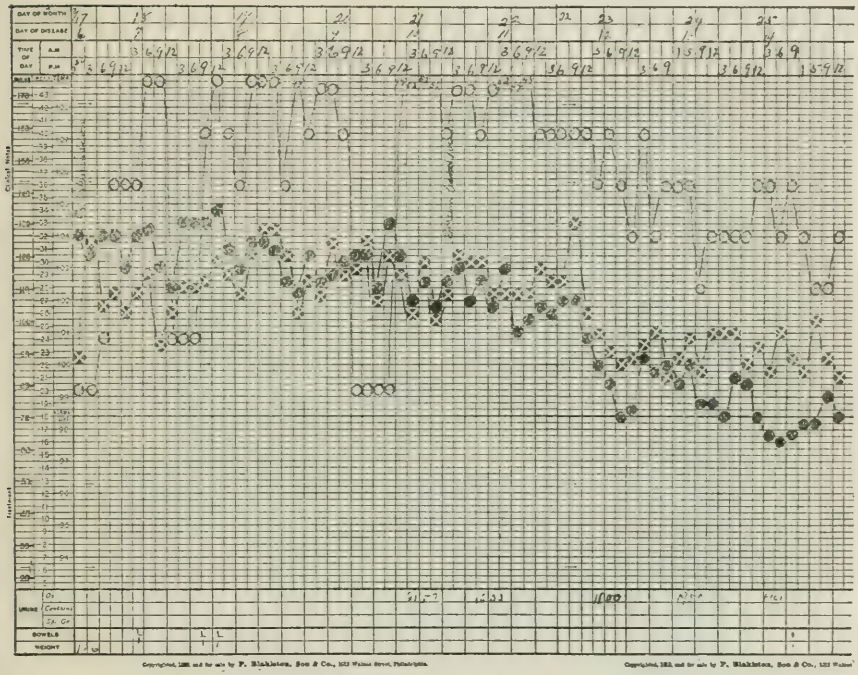

Fig. 95.—Case V. Lobar pneumonia. Serum (10 c.c.) intravenously on tenth day.

**Case VI.**—File No. 11,028. M. F. Aged twenty-eight years. Admitted 3/19/17. On 3/12/17 severe headache which obliged him to stop work. During the night intense pain in left chest interfering with breathing and short hacking cough with blood-streaked sputa. Chest strapped, causing relief.

Physical examination on admission showed pneumonia of the left lower lobe. Blood examination: 15,300 leukocytes and 83 per cent. neutrophils. Sputum characteristic; pneumococcus Type II. Temperature from 3/19 to 3/21 continuous from 101° to 103° F.

3/21: Physical examination of left base as before; upper lobe now somewhat impaired.

At 12 M. (eighth day): 10 c.c. of serum intravenously. Temperature subsequently rose from $101\frac{2}{5}°$ to 103° F. at 6 P. M., then rapid crisis to normal at 12 M. the following day. No subsequent elevation.

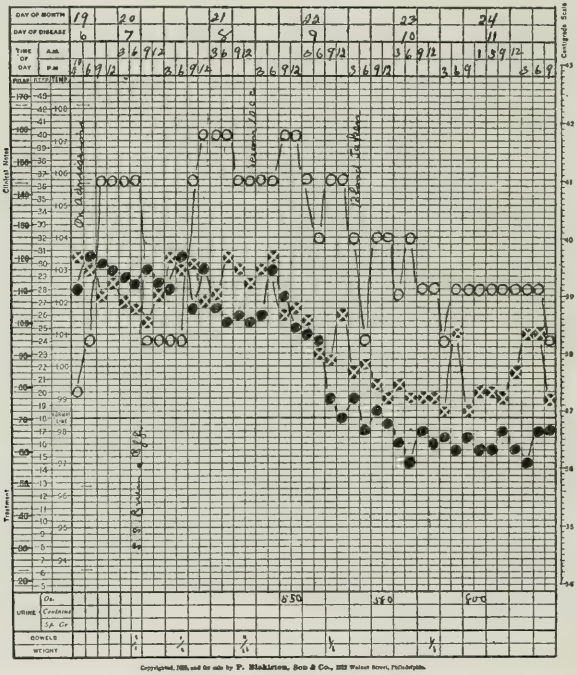

Fig. 96.—Case VI. Lobar pneumonia. Serum (10 c.c.) intravenously on eighth day.

3/22: Râles of resolution and evident decrease in the physical signs.

Complete and uninterrupted resolution.

**Case VII.**—File No. 11,043. J. G. Eighteen years. Admitted 1/8/17. On 1/5/17 had nausea and vomiting and stopped work. Following day had severe cough and pain in right chest, free expectoration of bloody, yellowish material.

Physical examination showed slight jaundice; pronounced

consolidation with other signs of pneumonia of right base. Blood examination: 7800 leukocytes, 85 per cent. neutrophils. Urine contained bilirubin. Sputum hemorrhagic and bile tinged. Temperature continued at about 103° F.

1/9/17 (fifth day): At 6 P. M. 10 c.c. of serum injected. Temperature fell during the night from 102° to 100° F., but rose the next day to 100° F., where it remained for three hours

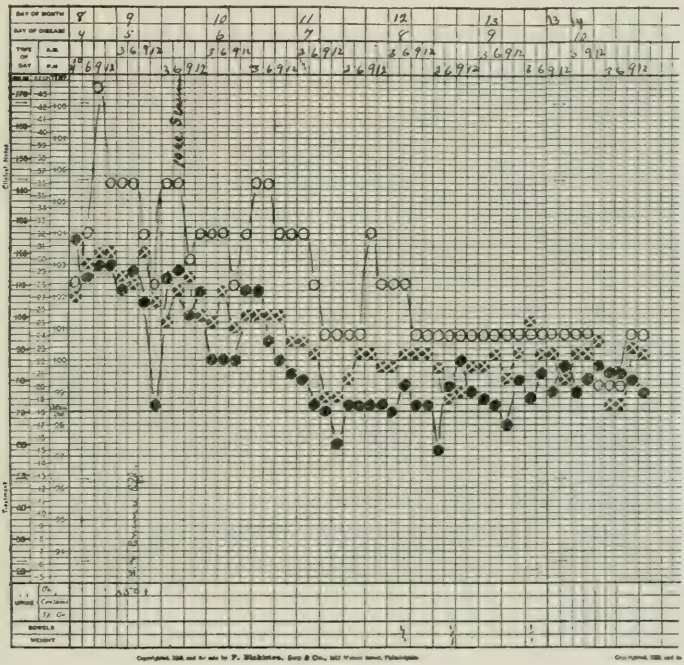

Fig. 97.—Case VII. Lobar pneumonia. Serum (10 c.c.) intravenously on fifth day.

and then fell by rapid crisis to normal, remaining normal until two weeks later, when he had a slight acute tonsillitis with fever lasting thirty-six hours.

Resolution of lung progressive and uninterrupted after crisis.

**Case VIII.**—File No. 10,057. E. G. Nineteen years. Admitted 2/26/17. Illness began 2/22/17 with a severe chill lasting three hours, followed by shortness of breath, and two

days later by pain in side requiring strapping. Unproductive cough. Physical examination showed marked consolidation and other signs of pneumonia in the left lower lobe. Blood examination: leukocytes 14,800, 82 per cent. neutrophils. Temperature on admission 104° F., but fell during the night to 101° F., and rose the next afternoon to 104° F.

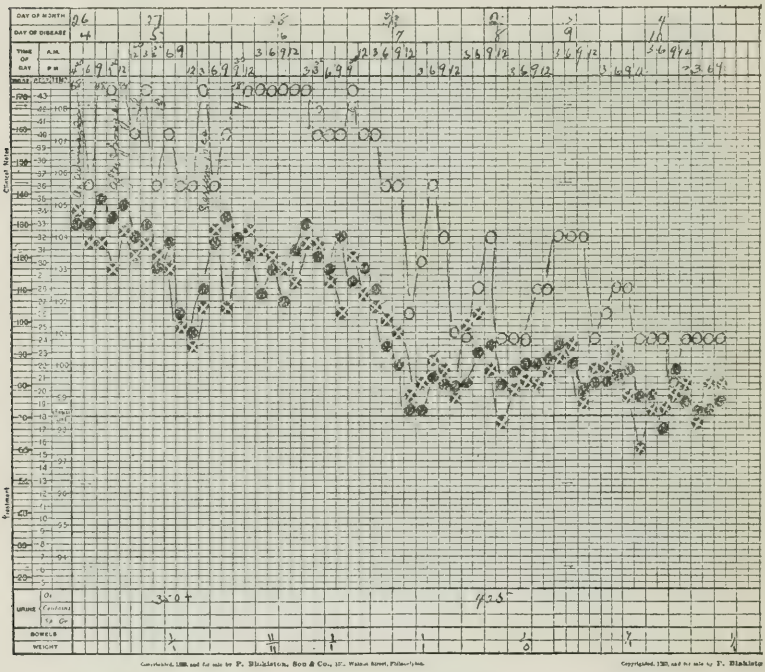

Fig. 98.—Case VIII. Lobar pneumonia. Serum (10 c.c.) intravenously on fifth day.

2/27/17 (fifth day): At 3 P. M. 10 c.c. of serum injected. Temperature fell from 104° to 102° F., but rose again the following afternoon to 104° F., then rapid crisis to normal. Subsequent to this there was rapid resolution with disappearance of pneumonic signs.

**Case IX.**—File No. 10,973. J. C. Aged forty-four years. Admitted 12/14/16. Illness began 12/10/16 with severe chill

on returning home from work, followed by pain all over body; later severe chest pain on breathing. Rusty sputum.

Physical examination on admission showed pneumonia of the right lower lobe.

Blood examination: Leukocytosis 7100, neutrophils 82 per cent. Urine negative.

12/16/16: Leukocytes 9900, neutrophils 85 per cent.

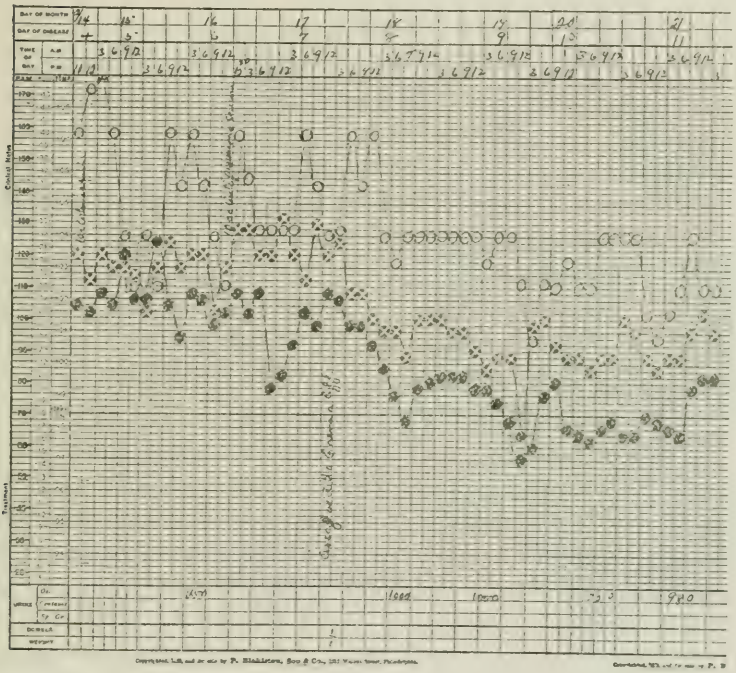

Fig. 99.—Case IX. Lobar pneumonia. Serum (10 c.c.) intravenously on sixth day.

Temperature on admission 102° F.

12/16 at 12.30 P. M. (the sixth day of disease): 10 c.c. of serum injected intravenously. Temperature fell to 99° F. at 9 P. M., and during the night rose again to 102° F.

12/17: After reaching 102° F., temperature again rapidly fell to subnormal. Convalescence subsequently uninterrupted.

You will observe that of the 8 cases in this series, all of which

were typical instances of lobar pneumonia, 7 recovered and 1 died, a mortality of $12\frac{1}{2}$ per cent. The fatal case was a double pneumonia, in a distinctly alcoholic subject of poor development (strabismic and underdeveloped), and when admitted was in a highly unfavorable condition (active delirium). The immediate effect of the injections of serum is better shown in the charts accompanying the case reports than can be brought out in further discussion. In practically all of the cases some immediate effect from the injection seemed to be evident. In 3 some slight increase of temperature suggesting a protein reaction occurred after the injections, but was followed soon afterward by a rapid crisis. In the other cases speedy decline of the temperature followed the injection and subsequent convalescence of the patients was prompt and complete. In 3 of the cases a moderate increase in the leukocyte count followed the injection, but in the other cases rapid diminution in the leukocyte count was observed. There were but 2 cases in which the type of the disease was recorded—1 case a Type I infection in which immediate effect was obtained from the use of the serum, the other a Type II case, with equally satisfactory result.

Though our results were highly encouraging we discontinued the method of treatment during the subsequent year owing to our desire to have cases more accurately typed and practical difficulties standing in the way. Subsequently curtailment of the staff owing to the war conditions prevented resumption of this line of investigation, until the epidemic of influenza in the fall of 1918 and the early part of 1919, and the unsatisfactory results of other methods of treatment suggested to us the resumption of a similar plan for the treatment of influenzal pneumonias. In the earlier period of the epidemic of influenza during September and October, 1918 the enormous numbers of cases that came under our care and the depletion of our hospital staff made it impossible to follow up this work except in a few cases, but in the early part of 1919, when the epidemic had waned and only moderate numbers of cases were admitted, we found it possible to resume this study.

The question of the possible usefulness of serum of con-

valescent influenza patients, of course, hinges on the probability of there being a real immunity and of the occurrence of immune bodies in the blood after this disease. Older authors assert that there is rather a predisposition to subsequent attacks than an immunity, and numerous reports of repetitions of the disease in the same individual and of recurrence in considerable proportions of large numbers of persons previously known to have had the disease have been published. To a certain extent recurrent attacks may be attributed to postinfluenzal conditions (persistent bronchial infection, bronchiectasis, etc.), but in a large series of cases in which considerable numbers of people have suffered from subsequent attacks a year or more after previous seizures, this explanation cannot be regarded as having weight. Jordan and Sharp (Jour of Infec. Dis., 26, 463, May, 1920) have shown that among the men at the Great Lakes Naval Station and at Camp Grant 19.8 per cent. among 1502 who had had influenza twelve to fifteen months previously had severe attacks in 1920, while 17.9 per cent. of 4875 who had not had previous attacks were affected. The conclusion from this large series of cases is obvious, that there is not a pronounced immunity at this interval after preceding attacks, though, as the authors properly observe, it does not prove the absence of immunity at earlier periods. In this connection it may be well to recall that formerly pneumonia, like influenza, was regarded as a disease which instead of conferring immunity rather predisposes to subsequent attacks. At present the proof of temporary immunity and of immune bodies in the blood after pneumonia cannot be questioned, and there is ground for believing that a similar temporary immunity occurs in the case of influenza, though equally convincing proof cannot be brought forward.

At the time when we were beginning to take up the question of immune serum in influenzal pneumonia based upon our previous experience in lobar pneumonia, other clinicians also occupied themselves with the same problem, and a brief review of their reports will be of interest.

McGuire and Redden made a preliminary report (Jour. Amer.

Med. Assoc., vol. 71, p. 1311, Oct. 19, 1918) on the use of immune serum in the treatment of influenzal pneumonia and published a second report (Ibid., vol. 72, p. 709, March 8, 1919). The final report gives the data in 151 cases seen at the Naval Hospital, Chelsea, and embraces all cases of influenzal pneumonia admitted to the wards since the treatment was begun, including the 37 cases of the first report. In the tabulated statement of the time of administration of the serum, it is shown that in 36 treatment was begun on the first day of the pneumonia, in 59 on the second, in 25 on the third, in 14 on the fourth, and 17 on later dates. The number of injections were as follows: 1 in 56, 2 in 49, 3 in 27, 4 in 9, and 5 to 7 in the remaining 10. The temperature became normal in less than twenty-four hours in 27, in twenty-four hours in 56, in two days in 38, in three days in 14, in four days in 8, and in from six to eleven days in the remaining 5. Of 138 cases, 83 recovered by crisis and 55 by lysis, the term "crisis" being used to indicate a drop of temperature to normal within twenty-four hours accompanied by general improvement.

They state that they have considered as influenzal pneumonia all cases with physical signs of pneumonia and a white blood count of 10,000 to 12,000 or less. If the white blood-count was higher, typing of the sputum was done. Even if the count was high and pneumococci of Group IV were found, the convalescent serum was used.

They make a supplementary report on the treatment of cases from the U. S. S. Tacoma which, coming from Bermuda November 5th, developed influenza at New London, November 18th, and sent to the Chelsea Hospital 77 cases out of a total of 80 cases of influenza in a crew of 96. Of the 77 patients sent to the hospital, 20 developed pneumonia, and all of these received immune serum as soon as the diagnosis was made. One patient had a complicating Type I pneumococcus infection for which the appropriate serum was given; 2 later developed streptococcic infection, 1 of them with empyema. There was one death, or 5 per cent. mortality.

*General Summary.*—Of the 151 cases, 3 died without complication and 3 after developing streptococcus empyema.

Incomplete experiments with pooled normal serum and with pooled serum from uncomplicated influenza patients indicate a lack of curative power in such sera. Pooled serum from patients treated with normal serum seems to have about the same potency as that from the earlier untreated cases.

After their first communication they advised (Jour. Amer. Med. Assoc., vol. 71. p. 1765, Nov. 23, 1918) that it was unnecessary to make compatibility tests of the blood before injections, and in their later report state that they have not observed chills, and have never seen urticaria or any other signs of serum sickness.

Lajoie (Jour. Lancet, 38, 657, Nov., 1918) reports 1 case with rather striking result after injection (intramuscularly) of 50 c.c. of citrated blood and 150 c.c. intravenously.

Machlachlan and Fetter (Jour. Amer. Med. Assoc., vol. 71, No. 25, Dec. 21, 1918) report their results with the use of citrated blood in the treatment of pneumonias following influenza. As a rule, they used 75 c.c. of blood, and four injections were the most that they gave to any one patient. In all, 93 injections were given to a total of 54 patients, all of whom represented severe influenzal infections with pneumonia. The milder types of infection were reserved as donors of blood—34 of their patients recovered, and 20 died. Of the fatal cases, there were 7 who were in the terminal stages when injected; and death occurred in all of these within twelve hours after the injection.

Ross and Hund (Jour. Amer. Med. Assoc., vol. lxxii, p. 640, March 1, 1919) report a series of 49 cases, 28 of which were treated with citrated immune blood and 21 cases symptomatically. The mortality of those treated with serum was exactly half (21.4 per cent.) of that of the series treated symptomatically (42.8 per cent.).

They used from 250 to 500 c.c. of the whole citrated blood at a dose.

O'Malley and Hartman (Jour. Amer. Med. Assoc., vol. lxxii, p. 34, Jan. 4, 1919) reported a series of 46 cases treated with citrated plasma in which there were but 3 deaths (6.5 per cent.)

Their average (untreated) mortality was 25.2 per cent. (111 patients). They followed the technic of McGuire and Redden, giving 125 c.c. of the citrated blood at a dose.

W. L. Brown and B. L. Sweet (Jour. Amer. Med. Assoc., vol. lxxi, No. 19, Nov. 9, 1918) report the use of citrated blood in 2 cases, both of which recovered.

### 1918–19 SERIES OF INFLUENZAL PNEUMONIA[1]

Our own experience was limited to 12 cases, 9 of which were regarded as influenzal bronchopneumonia and 3 as lobar pneumonias associated with influenza. It is, of course, obvious that in a civil hospital routine treatment of this sort cannot so readily be carried out as in a military establishment where the management of the material is so much more completely under the control of the physicians. In many cases we found it difficult to obtain blood from convalescent patients when particularly desirable, and were thus prevented from having a supply of blood or serum at times of greatest need. This difficulty, of course, will always occur, and is naturally one of the principal drawbacks in this method of treatment. A review of the experience we had during the influenzal period may now be recited.

**Serum Donor, Case B.**—On January 5, 1919 a patient was admitted with typical influenzal pneumonia. The onset had been gradual, with muscular pains and pronounced malaise. There was no initial chill, nor were there pleuritic pains. The white cell count was 4600. Physical examination showed scattered râles at both bases with bronchial breathing. The patient's recovery was prompt and uneventful. Nine days after the temperature was normal (January 18, 1919) 150 c.c. of blood were removed for the purpose of obtaining immune serum. Diagnosis: Influenzal pneumonia.

**Case X.**—On January 26, 1919, H. D., a woman aged twenty-four, was admitted to the ward after four days' illness in which

[1] I wish to express my thaks to my intern, Dr. Francis Grant, for his enthusiastic help in the treatment of the influenzal series and in the preparation of the case reports of this group.

she had suffered from severe pains in the back and limbs without initial chill or sore throat. There was a hacking cough and on examination of the chest impairment in percussion with harsh breath sounds and abundant râles at both bases were discovered. The blood count showed 7120 leukocytes and 60 per cent. neutrophils. Her temperature ranged from 101° to 104° F. On the third day in the hospital or the sixth day of the disease she was given 30 c.c. of immune serum from the patient above referred to (Case B). The temperature at the time of injection was 102.4° F. On the seventh day of the disease within thirty-six hours of the administration of the serum her temperature was normal and the subsequent recovery was uneventful. Six days after her temperature was normal 150 c.c. of blood were removed from a vein for the preparation of serum. Diagnosis: Influenzal pneumonia.

**Case XI.**—On February 6th I. R., aged thirty-five, was admitted to the women's ward, having been ill four days with severe headache following a sharp chill at the onset. She had had some cough for a week or two before. There was considerable dyspnea and blood-streaked sputum. On physical examination marked impairment of the right base was found on percussion and large moist râles throughout both lungs. The blood count showed 9600 leukocytes with 92(?) per cent. neutrophils. The exact date of onset was difficult to determine owing to the preceding cough or cold, but it was supposed that the day of admission corresponded with the ninth day of the disease. Her temperature continued from 101° to 103° F. up to the eleventh day, when she received 25 c.c. of serum from the original case (Case B). Within twenty-four hours her temperature was normal and convalescence was apparently established. Diagnosis: Influenzal pneumonia.

**Case XII.**—E. P., aged thirty-three, was admitted to the women's ward on February 6th, having been ill for four days with severe aching pains beginning in her legs and extending over the entire body. She had had severe headache and bloody expectoration and there were fine râles on both sides, mainly at the bases. The right base was impaired on percussion and the

breathing was distinctly harsh, approaching a bronchial character. At the left base the breathing was harsh, but there was no dulness. The leukocyte count was 3400 with 71 per cent. neutrophils. Her temperature from the time of admission ranged from 101° to 104° F. On the sixth day, with a temperature of 103.2° F., she received 50 c.c. of serum from Case XI, which was followed by an almost immediate crisis and the temperature was normal thirty-six hours after the injection. Within twenty-four hours following the crisis she was bled 500 c.c. for the preparation of serum. Her temperature remained normal six days, but she then developed a pleurisy with return of fever which lasted for ten days and ended in an uneventful recovery. Diagnosis: Influenzal pneumonia.

**Case XIII.**—Mrs. S. H., aged thirty-four, had had a severe pleuritic pain following exposure two weeks prior to admission, and since that time had been more or less ailing. Four days before admission she had a sharp chill with renewal of pleuritic pains, fever, headache, dyspnea, bloody sputum, and an eruption of herpes about the mouth. Physical examination after admission to the hospital showed some impairment of the left upper lobe and fine moist râles throughout both lungs. At the left base breath sounds were somewhat feeble or suppressed, while at the right base there was dulness on percussion and bronchial breathing. Leukocytes 20,200, neutrophils 96 per cent. Her temperature ran steadily at an elevation of between 101° to 102° F. On the fifth, eighth, and ninth days of the disease she received 30 c.c. of serum from Case XI. There was a moderate fall of temperature after each injection and a crisis within twenty-four hours following the last. Within a day or two after the crisis the temperature rose again, with the development of empyema, for which thoracotomy was done. The patient eventually recovered. The condition of the patient at the time she received the serum injections was desperate, as her dyspnea and cardiac weakness were out of all proportion to the degree of temperature. Following each injection there seemed to be a material improvement in the clinical appearance of the patient, and after the second there was a sharp reactive leuko-

cytosis—41,500. Notwithstanding the apparent improvements after the injections, the beneficial effects of serum seemed less definite in this case than in others, and the final crisis quite probably occurred spontaneously as it might have done without the treatment administered. Diagnosis: Lobar pneumonia.

**Case XIV.**—A. P., aged ten, a son of Case XII, was admitted to the children's ward on February 23d. His illness had begun with a sudden sharp chill, cough, pain and hemoptysis, and there was marked consolidation of both lower lobes with diffuse râles throughout both lungs. The leukocytes numbered 14,500 and there was 83 per cent. neutrophils. On the ninth day after his admission he was given 30 c.c. of serum from Case XI, but was practically moribund at this time and showed no improvement following it. Death occurred twenty-four hours later. Diagnosis: Lobar pneumonia.

**Serum Donor, Case C.**—N. P., aged twenty-six, admitted March 6th. Had been ill for one week, suffering from frontal headache, weakness in the lower extremities, myalgic pains, nausea, and fever. There was very little cough or expectoration, but on percussion impairment was found at the right base and bronchial breathing with fine moist râles were heard. Diffuse râles without marked change in breath sounds were heard throughout the remainder of the right lung. The leukocytes numbered 8700, the neutrophils 86 per cent. His temperature fell to normal three days after admission and he was bled 600 c.c. forty-eight hours after the temperature had become normal.

**Serum Donor, Case D.**—Mrs. S. S., aged forty-two, had taken cold a week before admission and four days later suffered from severe headache, chill, generalized muscular pains, and fever. Her lungs on admission showed harsh moist râles on both sides, without definite percussion dulness. The leukocytes were 6400, neutrophils 71 per cent. Her temperature ranged from 101° to 104° F. and declined rapidly on the third day after admission, reaching normal in thirty-six hours. She was bled 300 c.c. for immune serum.

**Case XV.**—M. T., aged twenty-five, seen in consultation with Dr. Ullom. She had been ill for four days with a slight catarrhal

(influenzal?) cold following exposure. After forty-eight hours she developed extreme muscular pains, cough, marked dyspnea, and high fever. When I first saw her on the fourth day her temperature was between 104° and 105° F., pulse 100, respirations 28 to 32. Cyanosis was marked and the examination of the

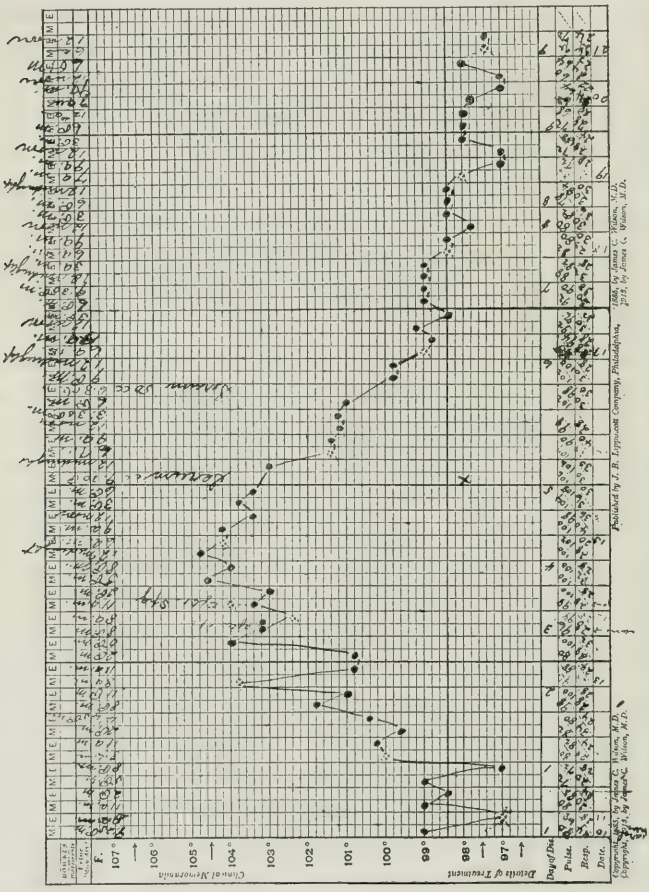

Fig. 100.—Case XV. Influenzal pneumonia. Serum (50 c.c.) on fifth and sixth days each.

chest showed indefinite dulness at both bases and abundance of coarse moist râles. The breathing was harshly bronchovesicular, but not clearly bronchial. The skin was leaky and the patient's general condition seemed desperate. On the fifth and sixth days of the disease, temperature remaining between 103° and 104°

F., she received two injections of 50 c.c. each of pooled serum from Cases C and D. Immediately following the first dose there was a critical decline of temperature to 101° F., where it remained for ten hours, when the second dose was administered. Following this a further crisis took place and the temperature reached normal in twelve hours. After this there was a rapid convalescence. Diagnosis: Influenzal pneumonia.

**Case XVI.**—Mrs. deA., also seen outside the hospital, had been ill for seven days. She was deeply cyanotic and dyspneic. The onset of her illness had been gradual, with malaise and muscle pains, followed by cough, shortness of breath, and expectoration. Diffuse uncertain consolidation at both bases with abundant moist râles and bronchial breathing were found on physical examination. On the seventh and eighth days she received 40 c.c. of serum obtained from her husband, who was a recent convalescent from influenzal pneumonia. The patient's general condition improved distinctly after the serum injections and her temperature began to decline, but did not reach normal until four days later. Five days after the temperature was normal fever recurred with signs of pleurisy. The patient then made an uneventful recovery. Diagnosis: Influenzal pneumonia.

**Case XVII.**—M. B., aged twenty-five, admitted to the men's ward March 10th. A week previously he had had pleuritic pains followed by severe cough, shortness of breath, mucopurulent expectoration, and fever. On admission complete consolidation of the left lung and evidences of bronchitis of the right side were discovered. Leukocytes 12,600, neutrophils 90 per cent. On the third day after admission, and probably the seventh day of the disease, he was given 70 c.c. of pooled serum from Cases C and D. There was a severe reaction with a chill lasting about an hour. Within forty-eight hours his temperature had fallen to normal. Type II pneumococci were found in the sputum. After a week of normal temperature he developed empyema and was operated on, with eventual recovery. Diagnosis: Lobar pneumonia.

**Case XVIII.**—Mrs. M. Z., aged twenty-nine, was seen at the Jewish Hospital with Dr. Ludwig Loeb. The patient was

in the eighth month of pregnancy. She had been sick for one week previously and had gradually grown worse; severe headaches, muscle pains, prostration, with increasing cyanosis and excessive dyspnea were the striking symptoms. Her temperature was low, ranging between 100° and 101° F. The pulse from 90 to 120, the respirations from 40 to 60. When I saw her she was deeply cyanosed, breathing was excessively rapid and shallow, and the patient suffered from a suppressed cough with expectora-

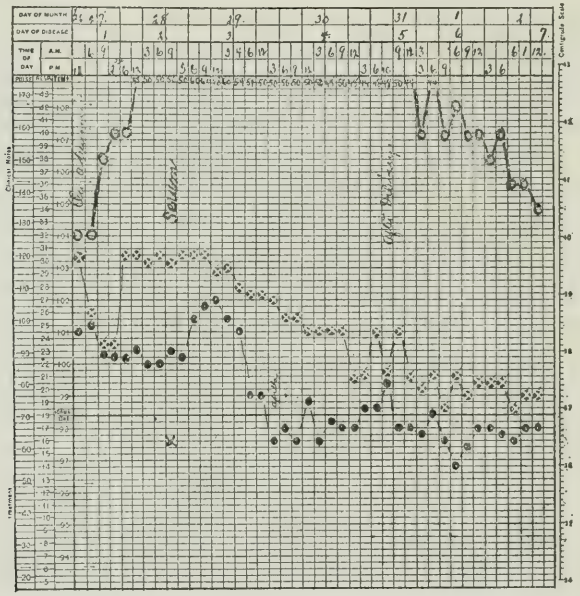

Fig. 101.—Case XVIII. Influenzal pneumonia. (Serum (30 c.c.) intravenously on third(?) day.

tion of bloody tinged, seropurulent fluid. There was also some hemorrhagic vomiting. Indefinite consolidation of the right base and abundant moist râles and suppressed breathing throughout both lungs were found on physical examination. She was given 30 c.c. of serum obtained from a convalescent influenzal pneumonia case. A moderate reaction with increase of her temperature from $100\frac{2}{5}°$ to 102° F. followed, and immediately after this a rapid crisis, the temperature reaching normal within

twenty-four hours after the injection. The whole picture of the condition changed and the patient's recovery followed. Two days after the crisis she was delivered of a dead fetus. Diagnosis: Influenzal pneumonia.

**Serum Donor, Case E.**—Aged thirty. Admitted April 10th to the Women's Medical Ward. A week before, after exposure, the patient had suffered from muscle pain, sore throat, and headache, followed by cough, expectoration, dyspnea, and cyanosis. Diffuse patches of bronchial breathing and râles with indefinite consolidation at the right base and left apex were found on physical examination. Leukocytes 5800, neutrophils 75 per cent. Her temperature declined rather rapidly, reaching normal on the seventh day. Five days later 250 c.c. of blood were removed for serum.

**Case XIX.**—I. W., female, aged sixteen, was admitted to the Medical Ward April 16th. Three days before admission she suffered from sore throat and general muscle pains. Two days later there was a slight chill, followed by fever, pain in the left chest and cough, with some mucopurulent expectoration. Diffuse signs with uncertain bronchial breathing and abundant râles were found at both bases. Subsequently marked impairment of percussion was found on the left side posteriorly and the breath sounds were clearly bronchial. On the right side sonorous and fine moist râles were heard throughout. Leukocytes 14,000, neutrophils 88 per cent. The temperature ranged from 101° to 103° F., the pulse from 110 to 130, respirations from 30 to 50. Upon the sixth and seventh days after admission, clinical conditions having gradually increased, 30 c.c. of serum from Case E were administered. Her temperature at the time of the first injection was 102.5° F.; following this injection there was a rapid decline of temperature to 99° F. followed by a reactive rise to $100\frac{2}{5}$° F., at which time the second injection was administered. After this injection the temperature rose to 102° F., but immediately declined by rapid crisis, reaching 99° F. in twenty-four hours, and subsequently, with slight recurrences, to 100° or $100\frac{2}{5}$° F., became normal in three or four days. Her sputum showed Type IV pneumococci. There was a moderate urticarial

rash following the second injection. Three days after the temperature became normal she was bled 300 c.c. for serum. Diagnosis: Influenzal pneumonia.

**Case XX.**—Mrs. L. M., aged forty-one, admitted to the Women's Ward April 24th. Four days previously muscle pains, sore throat, and a pleuritic stitch on the right side, followed by dyspnea and cough, mild chilliness, fever, mucopurulent, and at times blood-stained sputum and cyanosis. On physical examination percussion showed dulness from the right base to apex posteriorly with fine râles and bronchial breathing; coarser râles were scattered through the left chest. The temperature ranged from 101° to 104° F. Leukocytes 12,000, neutrophils 78 per cent. On the fourth day of the disease (temperature 103° F.) 60 c.c. of serum from Case X were given. A slight drop in temperature followed by a reactive elevation to the previous level and then by a critical decline to 100° F. was observed after the injection. A second elevation of the temperature occurred immediately after this to 103° F., when an intravenous injection of 250 c.c. of 5 per cent. sodium bicarbonate solution was given. There was a sharp crisis following this and the temperature declined from 103° to 96° F. in six hours. No unfavorable symptoms were observed during this crisis. During the next twelve hours the temperature again rose rapidly to $102\frac{2}{5}$° F., but immediately fell again to the normal, where it remained until convalescence was completed. The sputum showed Type IV pneumococci. Diagnosis: Influenzal pneumonia.

**Case XXI.**—Mrs. B. K., aged thirty, admitted October 28, 1918, had fallen ill on October 25th with cough and pain in the right chest, headache, myalgic pains, and vomiting. On physical examination distinct impairment on percussion and slight bronchial breathing were detected at the left base and suppressed breathing throughout the right lung. Subsequently numerous moist râles were heard, especially on the left side, and the evidence of consolidation of the left base became more distinct. The temperature ranged from 102° to 104° F. The pulse-rate was from 80 to 105, respirations from 27 to 40. The leukocytes

numbered 6600, neutrophils 58 per cent. On October 30th, the fifth day of the disease, 40 c.c. of serum were injected, following which the temperature declined to 100° F. in twenty-four hours and to the normal twenty-four hours later. Convalescence was uninterrupted.

In one other case, a woman aged forty-four, with presumably influenzal pneumonia, 75 c.c. of serum were administered, but the patient succumbed. As this case was admitted in a practically moribund state and died ten hours later I have omitted it from the tabulated list of cases. Two other cases in the series were practically in a desperate state when admitted, but as death was not so immediately imminent I felt it right to include those, though they seemed wholly unfavorable at the time.

In reviewing the 12 cases of this series we regarded 9 as simple influenzal pneumonias and 3 as lobar pneumonias in patients probably suffering from influenza. I do not wish at this time to enter at length on a discussion of the nature of influenzal pneumonia. The prevailing opinion regarding influenza undoubtedly is that, whatever the original and specific cause of this disease, secondary infection later plays an important part and particularly in the cases terminating in pneumonia. There are, however, clinical and to a less extent bacteriologic grounds for believing that cases of pure influenzal pneumonia occur, and there is good reason for believing that the mere discovery of pneumococci or streptococci in the sputum of cases of influenzal pneumonia is insufficient evidence to prove that a mixed infection is necessarily present. In classifying our cases as either influenzal pneumonia or lobar pneumonia we have been governed by clinical rather than bacteriologic considerations; and have been influenced mainly by the history, the character and extent of physical signs, and by the leukocyte count. Cases regarded as influenzal pneumonia have invariably shown diffuse physical signs, commonly bilateral, and always much less clearly marked than in lobar pneumonia, and the leukocyte count has usually been below 10,000, while the differential count has commonly shown a relative deficiency in neutrophils, or at least no increase.

The development of the signs of pneumonia is somewhat gradual and irregular, following a clear picture of ordinary influenza. On the other hand, the cases regarded as lobar pneumonia have had sudden onset of symptoms of pneumonia, a rapid development of physical signs with clearly marked lobar consolidation. The leukocyte count was above 12,000 and the proportion of neutrophils marked (80 to 90 per cent.). Of the 12 cases reported here, 9 were regarded as influenzal pneumonia and 3 as lobar pneumonia in influenza patients. It must be admitted that the existence of influenza in the latter was not entirely certain, though clinical appearances strongly indicated its presence.

All of these patients were seriously ill. In several the condition of the patients seemed well-nigh desperate. This was particularly true of the pregnant woman seen at the Jewish Hospital and to a somewhat less extent of Case XV. The 9 influenzal cases all recovered. Of the 3 pneumonias, 2 recovered, and Case XIV, a boy of ten, died. The clinical notes of the latter state that he was "deeply cyanotic, extremely dyspneic, and practically moribund" at the time serum was administered.

The injections of serum were given on from the sixth to the tenth day. In some instances it seems probable that resolution may have begun at the time of injections, though in every instance the clinical appearances did not indicate this, and the serum injections were used in the belief that the condition showed no evidence of relief. The dosage of serum varied from 30 to 70 c.c. In 2 cases a total of 100 c.c. were given; in 1, 90 c.c.; in 1, 60 c.c.; in 1, 70 c.c.; in 1, 50 c.c., and in the remainder single injections of 30 c.c. So far as we could observe no marked difference was apparent when the larger doses were used.

The serum used in these cases was derived from convalescent influenzal pneumonia cases and was only employed when a negative Wassermann had been reported. As far as our opportunities permitted the patients were bled as early as possible after convalescence, as we believed the antibodies more likely

to be present in abundance immediately following defervescence. We also selected cases in which the decline of temperature was more or less critical. Frequently this desire to obtain blood early was not fulfilled because of the condition of certain patients in the first few days following their convalescence.

The technic used in obtaining and preparing the serum was very simple. A needle connected by a rubber tube with a flask was introduced into the median basilic vein. The flask was provided with a side opening through which suction could be made, and thus the blood was aspirated directly from the vein into the sterile flask. After the serum separated it was carefully pipeted and placed in sterile containers and kept on ice. Cultures of the serum were made to insure the absence of microorganisms. In most instances our supply permitted us to use rather fresh serum, that is, serum within two or three days after it was prepared. In a few cases, however, the serum had been kept on ice up to ten days or two weeks. In most instances serum from a single patient was employed, but in a few, combinations, or pooled serum, were used. In only 2 cases did any reactions follow—in one a rather marked urticarial rash, in the other (a pneumonia case) a severe, but brief, chill. In the earlier series of cases (lobar pneumonias) the dosage of serum was relatively small, sometimes only 10 c.c. Doubt may naturally arise regarding the possible effects of such small doses, but the prompt crisis (occurring in cases treated as early as the fifth or sixth day of the disease) is, to say the least, suggestive.

It is, of course, impossible to draw any conclusions from such small groups of cases, and no attempt will be made to do so. The results must be taken as suggestive of a possible means of combating forms of diseases for which other modes of treatment are rather inadequate.

The first series of cases, which were pure lobar pneumonias, occurred at a time when influenza was not prevalent and had no relation to the second series. The results obtained were undoubtedly striking, and it was our intention to follow up with a larger investigation. Unfortunately, during the following winter conditions occurred as a result of the depletion of hospital staffs

that made it impossible to carry out this intention, particularly as we hoped to test the value of the treatment in different types of pneumonia, and the proper bacteriologic study of the cases was then impossible. Moreover, our material during the following winter was rather scanty. The occurrence of the influenza epidemic in the fall of 1918 and of influenzal pneumonias gave an opportunity for renewing these studies. At the height of the epidemic we were unable to carry it out, as at that time our limited staff was extremely hard pressed to fulfil their routine duties, but after the peak of the epidemic was passed and the cases of influenza and pneumonia became a little less abundant we were enabled to treat a few in this manner. It must be recognized that at the time of the treatment of these cases influenzal pneumonia was less rapidly fatal and the percentage of fatalities was undoubtedly smaller than during the September and October preceding, but there was still a very decided mortality, and the recovery of the series of 9 severe cases[1] is at least worthy of remark, although the number of cases is too small to justify any conclusions other than that the favorable results in these cases and the readiness with which this treatment may be employed when available material for obtaining the serum is at hand would warrant its use in similar cases. The published statistics from other places have been very encouraging, and it would seem desirable in case of another outbreak of influenzal pneumonia that this method should be employed upon a much larger scale than has up to this time been attempted.

The prevalence of lobar pneumonia at all times will give the opportunity for further investigation of the use of immune serum in this disease. It is not intended or suggested that the antipneumococcus serum that has been provided for Type I infections should be displaced by this form of treatment, but the inefficacy of alien serum in other types of pneumococcus infection would justify the employment of human immune serum in these cases.

[1] It is noteworthy that at least half of the cases treated with serum were those in which other methods of treatment had been used to the point at which their uselessness seemed apparent and a fatal termination was feared.

A number of reports have been published to show the possible value of injections of non-specific proteins in the treatment of influenzal pneumonia. Some of these reports indicate the possibility of usefulness from this method of treatment, but all show that preceding any favorable effort severe reactions, sometimes evidently grave in their possible effects, have occurred. It is a striking contrast in our cases that crises with rapid convalescence have occurred with no reaction whatever, save in the 2 cases mentioned, when trivial reaction was observed.

## CLINIC OF DR. THOMAS McCRAE

JEFFERSON HOSPITAL

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### PAIN IN THE LOWER BACK

THE reproach is sometimes brought against teachers of medicine that they give too much attention to the rarer conditions and neglect to instruct you in the more common, everyday maladies. Perhaps the reproach is justified, but whether it is or not, there is no doubt of the importance of your learning as much as possible of what are sometimes regarded as minor ailments. They may be so described by the onlooker, but the patient is not likely to regard them as such. My intention is to bring before you some examples not of a disease, but of a symptom which may be caused by many widely different diseases, namely, pain in the lower back. This sounds like a prosaic subject, but we may be able to find some interest in it. Certainly the complaint is common enough, and if we are to do anything more than give symptomatic treatment we must be able to decide as to the cause of the pain. The term "lumbago" is often given to pain in this region, usually associated with stiffness, but you will find it difficult to give any exact definition of lumbago and to accurately define the many conditions which are so diagnosed. It is a diagnosis which is easily made, but often does not result in benefit to the patient or satisfaction to the physician.

Pain represents irritation of the sensory nerves supplying the affected area or of a nerve which has some connection with them. The sensory division of the nerves involved here sends branches to the skin, the muscles connected with the spine, the spine itself, and the meninges and the viscera. The seat of pain and the cause of that pain are not necessarily in the same situation—a point never to be forgotten in the study of any form of pain.

In the study of pain in the lower back an important point is the presence or absence of tenderness on pressure in the area where the pain is felt. If the two coincide, it suggests that the diseased condition is localized, but if the contrary, that we are probably dealing with a "referred pain." In other words, the actual disease is elsewhere, but the sensorium refers the pain to this area. In this event we may find some disturbance of sensation over the area involved, which is usually hyperesthesia.

Let us take up the structures which may be responsible for pain in this region. It is evident that disease of the spine itself may be the causal factor. Injury, disease of the bones, joints or ligaments, or any process which involves the nerve roots may be responsible. The process may be in the sacro-iliac joint or there may be some anatomic peculiarity which causes trouble. Possibly there are conditions in the nerves themselves, which we call neuralgia, exactly as in the nerves elsewhere. Disease of the cord itself or of the cauda equina is another possibility. Disease of the meninges, not infrequently syphilitic, may involve the nerve roots and cause pain. Then there is the possibility of referred pain which may come from disease of the abdominal or pelvic organs. The pelvic organs are those more often responsible, and in this connection do not forget that there is pelvic disease in the male as well as in the female. The prostate and seminal vesicles are important sources of symptoms.

With one form of pain or discomfort in the lower back we are probably all familiar by personal experience—that which comes with severe physical fatigue. Of much more importance is the pain which occurs with nervous fatigue. You will find it a frequent complaint from nervous patients in whom the most thorough search fails to show a basis for it in any physical disease. We have to confess that in many such cases we have no satisfactory explanation as to the cause.

It is not probable that examples of all the forms of pain in the lower back can be demonstrated to you, but it should be possible to demonstrate some of them and show how necessary it is to make a complete study in each case. There should be enough examples to prove to you the wide variety of causes and how

many possibilities have to be kept in mind in the investigation of each case.

Before discussing the cases let us run over briefly some of the important points in the examination. This must be thorough, and the back, abdomen, pelvis, hip-joints, pelvic organs, and skin sensation should all be studied. The back should be bare; you cannot inspect it through a shirt. Examination, if possible, should be made with the patient standing so that the shape of the spine and its movements can be studied. Then he should be examined lying on the face and on the back. Particular search should be made for any deformity and the movements of the lower spine carefully tested. Care must always be taken to look for evidence of disease of the cord and cauda equina. The pelvic examination is important in both sexes and a rectal examination should never be neglected in the male. If there is any doubt, an *x*-ray examination of the lower spine, pelvis, and hip-joints should be made. Another point which should never be neglected is the study of the patient's station. He may "hold himself badly" as we say, that is, the shoulders are rounded and there is a lax sagging abdomen. The balance should be noted, and whether there is asymmetry in the legs. There may be flat-foot or, in the case of women, the balance may be disturbed by the wearing of badly designed shoes—usually with high heels.

### LUMBAGO

**Case I.**—The patient is a white male, aged fifty-eight, a clerk, who complains of severe pain in the lower back. His family history is negative and in the past history there is little of interest. He has been very healthy and since childhood has not been ill except with attacks similar to the present. There is no history of gonorrhea or syphilis and he has taken very little alcohol. As you see, he is rather corpulent and has been so for ten years.

*Present Illness.*—Five days ago he got up in the morning feeling perfectly well. While shaving, his brush fell on the floor. He stooped over to pick it up and was instantaneously seized with pain in the lower back. He describes it "as if someone had

run a knife in me." He was unable to straighten his body and had to remain bent over in a stooping position. He did not feel able to move and had to be helped back to bed. There he was propped up with pillows, as he could not lie down, and for a time the pain continued in a very severe form. Later in the day the pain became less, but he is still compelled to hold himself in a somewhat bent position and is unwilling to try to straighten the back or make any movement with the trunk which can be avoided.

He has had a number of similar attacks during the past seven or eight years, with an average of about one a year. The onset has always been very acute. One attack came on while he was lacing his shoes, another when he was lifting a heavy basket. The pain is of maximum severity and he says "it makes me helpless. I cannot do anything." He refers it to the lumbar region and states that it is present on both sides. There is some relief in a few hours, but it has been, as a rule, seven to ten days before he is free from discomfort. The pain lessens gradually, but any stooping motion is apt to bring it back.

*Examination.*—This is negative as regards the viscera, blood, and urine. It may be noted that there are no signs of gout. The only abnormal finding is in the lower back. You observe the attitude. The patient stands with the trunk held stiffly and bent forward somewhat. He sits down very carefully and slowly, and any attempt to twist the body causes pain. On examination, the muscles of the lower spine are held rigidly and there is pain when pressure is made over them. There is marked spasm of the muscles on irritation. There is no evidence of involvement of the sacro-iliac joints and the *x*-ray examination of the spine is negative.

*Diagnosis.*—What has occurred to disable this man so suddenly? The diagnosis must be made largely by exclusion. There is no evidence of disease of the spine, cord, joints, abdominal or pelvic organs. The process is apparently located in the lumbosacral region. This is occupied by a large mass of muscle, but of particular importance is the lumbar fascia. You will remember that this is the vertebral aponeurosis of the

transversalis and divides into three layers which enclose the quadratus lumborum, erector spinæ, and multifidus spinæ muscles. The symptoms and signs suggest some involvement of these structures. If so, what is involved? It must be either muscle or fibrous tissue. Myositis is a rare condition; fibrositis is common. In some patients with a similar condition we can find areas of induration and sometimes nodules after the acute features have subsided. In some patients during the acute stage we can feel areas which suggest serious infiltration. These findings suggest an inflammatory process in the fibrous tissue, and this seems the most reasonable view of the nature of this condition.

There is another point, namely, the result of local treatment by acupuncture. This consists in the introduction of sterile needles deep into the muscles, which are left in for five to ten minutes. In some cases, but not in all, this gives very prompt benefit. This may come by the relief of tension; it is difficult to see how it could act otherwise. This was a favorite method of treatment of the late Sir William Osler who learned it from Ringer. I have used it successfully in some cases.

There is also the history of previous attacks which were followed with complete recovery, and the course of this one should be of help. [The patient was seen some weeks later when he had completely recovered and showed no signs of any disease.]

We have much to learn regarding this condition. The term "lumbago," if used at all, should be restricted to this group, but as often employed it means nothing more than pain in the lower back. Such a diagnosis should be made only after every other cause has been excluded. So-called "chronic lumbago" should be looked on with suspicion. Possibly there may be such a condition representing a chronic fibrositis, but the majority of the cases are found to be due to something else, usually a bone or joint lesion. It is a diagnosis which I make with much hesitation, and yet it seems justified occasionally, as in this case. Certainly it is the last diagnosis to be made as to the cause of pain in the back, and only after all others seem to be excluded. Some writers lay great weight on the importance of gout in the

etiology, a doubtful point, in my opinion, in the majority of the cases.

The frequent influence in the etiology of some slight trauma is puzzling. The onset with a severe effort may suggest injury or tearing, but one is impressed by the frequency with which the attack comes on with some ordinary movement, such as bending. Exposure to cold or a wetting may precipitate an attack in some patients. Certainly one attack predisposes to subsequent ones, which, with the presence of thickening in some cases, suggests fibrositis, with resulting changes and a susceptibility to further attacks.

What is the etiology of the fibrositis? Naturally one thinks of a focus of infection and this should always be considered and search made for such. In one case after recurring attacks of "lumbago" for three years, the removal of an infected tooth resulted in a complete disappearance. After a period of four years there has been no return. Careful inquiry in these cases will sometimes elicit the fact that there have been attacks of pain elsewhere, as in the neck muscles or about the shoulders, which suggest fibrositis. But always be suspicious of a diagnosis of "lumbago" and look for something else back of it. Still the temporary duration of the attacks and the complete freedom from any symptoms between them suggest that there is such a disease. Until we have proof of something else the best plan is to regard it as fibrositis.

**Case II.**—This is of a somewhat different character, in that the pain has been persistent and has not come on in attacks. The diagnosis is more difficult and he is presented for comparison with Case I.

The patient is aged thirty-four, a male, and a laborer by occupation, who complains of pain in the lower back and inability to bend the body forward or to the right.

The past history seems practically negative. He has never had any acute infectious diseases. There is no history of any injury. He formerly used alcohol rather freely. He gives no history of syphilis or of gonorrhea. The present illness began about a year ago with pain in the lower right back. He described

it as being situated rather deeply. He kept at work for about six months, but then had to give up, and since then he has worked only an occasional day or two at a time. The difficulty of stooping and moving, and the pain which they cause, prevent him from working.

*Examination.*—The patient is a healthy, well-nourished man. The tonsils are enlarged and show evidence of infection. The upper parts of both lungs show changes rather suggestive of a fibroid character, probably with anthracosis. The heart is clear and the abdomen negative. As long as the patient is in bed he is perfectly comfortable. When he stands there is no visible deformity and he makes no complaint of pain. On bending backward, forward, and to the left there is no restriction of motion and no pain produced, but on bending to the right, and especially to the right and a little forward, there is evidently very sharp pain in the lower back which "pulls him up short," as you can see. The situation of the pain and his behavior on movement to the right suggest the possibility of a long transverse process of the last vertebra on the right side. There is no evidence of involvement of the sacro-iliac joints and no pain on pressure over the sciatic nerves. There is no tenderness in the region of the kidney and neither kidney can be felt. The urine is clear and the temperature and pulse normal. The blood count is normal, with 6800 leukocytes. The Wassermann reaction is negative. An *x*-ray study of the spine and sacro-iliac joints is negative as regards any gross change.

*Diagnosis.*—This offers difficulties and an exact conclusion is difficult, an important reason for showing the patient. Is this an example of lumbago? The duration, the situation of pain on one side, and the absence of symptoms except on bending are all against this diagnosis. The *x*-ray studies exclude any gross lesion in the bones. There is no evidence of disease of the kidneys or prostate or of the central nervous system. We must remember that there may be disease of the spine which does not give any marked signs that can be recognized in an *x*-ray plate. Is it possible that such is the case here? Fixation of the lower spine gives him relief, which is a suggestive point. If he has such a

lesion we believe it is secondary to a focus of infection somewhere. Such a focus exists in the tonsils and this raises the question of their removal. In any case he is better without infected tonsils, and he is willing to have them removed. [This was done, and marked infection found in both. He improved steadily and was discharged considerably better. Three months later he reports himself as practically well.]

*Remarks.*—It is difficult to make an exact diagnosis in this case. It seemed more like spondylitis than anything else, but exact proof is lacking. It may have been a fibrositis. Certainly the existence of some inflammatory process of a low grade is suggested by the therapeutic result, but we must leave it as of doubtful diagnosis. He has been advised to endeavor to obtain work which will not involve bending in order to avoid any strain from occupation.

### SPONDYLITIS

**Case III.**—The patient is a white male, aged forty-nine, admitted complaining of shortness of breath and pain in the lower back. There is no history of an acute infectious disease. He gives a history of having shortness of breath at times for about three years and of some frequency of urination. There is no history of any edema.

*Present Illness.*—This goes back for a period of about three years. During this time he has had shortness of breath, but he makes light of this and states that the reason for which he enters the hospital is persistent pain in the lower back. He points to the lumbar region as the seat of this and states that the pain does not radiate, is practically constant with exacerbations, and is always worse on exercise or moving. It has been difficult for him to do his work, which is that of laborer, for the last two years on account of the pain and disability. He has had a gonococcus infection at least on two occasions many years ago. There is no history of syphilis.

*Examination.*—The patient is poorly nourished and is evidently suffering pain. The most striking point in the examination of the thorax and abdomen is the state of the heart. There

is no marked dyspnea or cyanosis and the heart impulse is not particularly strong. There is increase in the dulness to the left and a well-marked to-and-fro murmur at the base, with the diastolic murmur unusually loud. There is a well-marked collapsing pulse and a marked variation between the systolic and diastolic pressures. There is no question about the presence of aortic insufficiency and of a good deal of myocardial change. The vessels do not show any marked sclerosis.

When the patient stands the spinal muscles stand out very markedly and on palpation are found to be firmly contracted. He is unable to stoop over and touch the floor. The patient complains of pain in the lower back more or less constantly and this is greatly aggravated by any movement. It is very evident that movement is extremely limited, particularly on bending forward and to either side. The leg reflexes are increased. The examination, therefore, shows that there is a very definite lesion in the circulation, aortic insufficiency, and, so far as we can make out, a spondylitis. We naturally think at once of the aortic lesion being syphilitic, and this is supported by the Wassermann reaction being strongly positive. The *x*-ray examination of the lower spine shows evidence of a slight grade of spondylitis. The changes in the bones and joints are not extreme, but are definite.

*Remarks.*—There can be no question as to the diagnosis of syphilis, and to this the disease of the aortic orifice is due without much doubt. There is also a strong suspicion that the condition of the heart muscle is probably influenced by the luetic infection. The point next arises as to whether this has played any part in the production of the spondylitis. It is difficult to prove this, and perhaps the therapeutic test offers us the best chance. We shall put the patient on mercury by inunctions and full doses of iodid by mouth, and study the result.

The patient was seen three weeks later. He is now entirely free of any pain in the back. Following the beginning of specific treatment there was a very prompt improvement and within a week the pain was materially less. After another week he was practically free of any pain. As it is most unusual for such a

result to occur in ordinary spondylitis, this seems to speak very strongly for it being syphilitic. This is a very striking and encouraging result of therapy. Keep in mind the possibility of every case of spondylitis being syphilitic until you have proved the contrary. Syphilis often attacks the bones and the result may not have any features suggestive of the diagnosis. But do not conclude that in every patient with spondylitis and a positive Wassermann reaction that the two are associated. A patient with spondylitis secondary to infection about the teeth or in the tonsils may have had syphilis in addition. The therapeutic test is sometimes our last resort in such a case.

### SACRO-ILIAC JOINT DISEASE

**Case IV.**—The patient is a white female, aged forty, who has been doing housework. Her main complaint is of severe pain in the lower back with marked nervousness and weakness.

In her *past history* there is a note of scarlet fever at seven without any complication, but no other acute disease. She has had one child, but no miscarriages. There has been no trouble with menstruation. Her digestion has been normal and the bowels, as a rule, regular.

*Present Illness.*—Eighteen months ago she was in an accident in which she was thrown violently on the pavement. She states that she was unconscious for some time afterward and that the left hip was very severely bruised, and, in addition, there was severe pain in the right hip and leg. She has had severe pain from that time until the present. As a result of the constant pain she has been able to do very little and has gradually become weaker. There has also been constant suffering and a resultant loss of sleep which she thinks accounts for her being so upset nervously. There has been a considerable loss in weight.

*Examination.*—The patient looks badly and is very thin and pale. Examination of the heart and lungs does not show any evidence of disease. The abdomen is negative and pelvic examination shows the pelvic organs in normal condition. The blood count shows a fairly marked anemia; hemoglobin 58 per cent., red blood-cells 3,800,000, leukocytes 6000. The Wasser-

mann reaction is negative. The urine has usually a normal specific gravity. On some occasions it has shown a small amount of albumin, but no casts. There are occasionally some pus-cells in the urine.

When we endeavor to examine the condition of the lower back we find that there is a very marked restriction of movement on account of pain. The patient turns in bed very slowly with extreme care, as any sudden movement gives her acute pain. On examination we find that there is considerable tenderness on pressure in the region of both sacro-iliac joints. It is impossible to extend the legs on the trunk on account of the severe pain caused by any effort to do this. Making pressure inward over the iliac crests causes severe pain. It is practically impossible to test the movements of the spine on account of the pain produced. Although a complete examination is difficult on account of the pain caused by movement there does not seem very much doubt that she has involvement of both sacro-iliac joints. She considers that the pain on the right side is more severe than on the left. The *x*-ray study supports this diagnosis. It does not show any evidence of a lesion in the lower spine, all the vertebræ appearing perfectly normal, but does show what are apparently definite changes in both sacro-iliac joints. There does not seem any question that in this we have the explanation for the severe pain which she suffers.

*Remarks.*—The anatomic diagnosis of the cause of the pain seems to be definitely made, but this leaves us with the necessity of trying to decide what is back of this and as accurately as possible the primary etiology. You will find it very difficult in many cases to decide as to the part played by injury in the production of disease. It is not difficult to understand that in this case the accident may have played a direct part. It is important, however, to look for other possibilities in addition to the trauma, and we find that she has a certain amount of infection of the tonsils.

As regards treatment, some form of fixation seems most likely to give relief. We had a specially reinforced corset made with the effort to try and give her as much fixation as possible.

This has given her some relief, but she is a long way from being well. It may be advisable to have the tonsils removed if she does not improve, but at present we are delaying to see the result of fixation.

With regard to sacro-iliac joint disease we have to remember that it is not always easy to be sure of the presence of minor grades of it. Where the process is as marked as in this patient, there can be little doubt. The *x*-ray examination is not always positive and does not, of necessity, show a slight lesion. The principal means of relief in these cases is some form of fixation.

### REFERRED PAIN FROM PROSTATIC DISEASE

We learn the lesson usually through sad experience that the seat of pain and the site of the disease causing it very often do not correspond. This patient is an example, and is an instance of another cause of pain in the lower back, which you will do well to keep in mind.

**Case V.**—The patient is a white male, aged thirty, a laborer, who complains of pain in the lower back. His past history shows that he had typhoid fever at the age of twenty, apparently a mild attack and without any complications. Four years later he had gonorrhea, the discharge lasting for some weeks, but after that time he regarded himself as well of the infection. Otherwise his history shows nothing of importance.

The present illness dates back about two years. At first the pain was present at intervals, but gradually became more constant and for over a year has been persistent. He has not noted any special factor which tends to aggravate or cause the pain. As a rule he has been free of pain at night. He does not think that stooping or bending renders the pain materially worse. At one clinic where he attended he was given a belt, but this did not benefit him. He states that occasionally there has been pain in the abdomen, but he cannot give any accurate account of this.

Before examining him let us see what we can get from the history. Mr. A., is there any comment you would make on this?

STUDENT: The history of typhoid fever.

DR. McCRAE: What bearing has that?

STUDENT: The possibility that he has typhoid spine.

DR. MCCRAE: That is perfectly correct, but you remember that an interval of eight years intervened between the attack of typhoid fever and the onset of the present illness. Such a thing is possible—for the typhoid bacillus may live in bones for many years—but not probable. If such is the case, what do you expect to find?

STUDENT: A spondylitis.

DR. MCCRAE: Correct, and the examination will settle that point. Mr. B., is there any other point to be noted?

STUDENT: The history of an attack of gonorrhea.

DR. MCCRAE: What may be the significance of that?

STUDENT: That he had a spondylitis due to the gonococcus infection.

DR. MCCRAE: That is also possible and the gonococcus is responsible for some cases of spondylitis. The odds are against a gonococcus infection having persisted for so long, but other organisms may have been added. There is no history of a second infection. Therefore, so far as the history is concerned, the suggestions are in favor of a spondylitis.

*Examination.*—The patient looks healthy and the examination of the thorax and abdomen shows nothing abnormal. The urine is clear, the blood count normal, and the Wassermann reaction negative. Now let us examine the spine with particular care. The movements are free in all directions and do not cause any pain. The *x*-ray plate of the spine is normal and does not show the least suggestion of any change. This seems to rule out spondylitis.

DR. MCCRAE: Mr. A., what would you examine next?

STUDENT: The sacro-iliac joints.

(Examination of these proved negative in every way.)

DR. MCCRAE: Are there any other suggestions? Spondylitis and sacro-iliac joint disease seem excluded. Mr. A., what do you think of the possibility of lumbago?

STUDENT: The prolonged course is against it.

DR. MCCRAE: It certainly is, at any rate if we limit the use of the term to the condition which we have studied previously and

called lumbago. There is another examination which may aid us, and that is of the prostate. This is found to be enlarged, and you can see that it is evidently tender, for even with gentle pressure on it he complains of severe pain. There is also some tenderness on pressure on the deep urethra suggesting some disease there. We have here a possible source of the pain in the back, and this is strengthened by the patient stating that he felt the pain in the back when pressure was made on the prostate and deep urethra.

Subsequently it was found that the verumontanum was inflamed and very tender when touched through the urethroscope. The patient was treated by prostatic massage and applications were made to the verumontanum. Improvement was slow, but it was steady, and when seen some months later the pain in the back had disappeared.

*Remarks.*—This patient is a good example of the necessity of full knowledge of the importance of referred pain. You have seen another case with prostatitis in which the pain was referred to the sciatic distribution and the patient came with the label of sciatica. Another error which the pain from a diseased prostate may cause is to suggest the diagnosis of renal colic. There are a number of such cases in the literature. The lesson is to make a thorough examination and to rest content with nothing short of it.

## CONCLUSIONS

These 5 cases which we have studied are examples of fairly common causes of pain in the lower back. There has not been great difficulty in the diagnosis of any one of them when a thorough examination was made. It may be of interest to note some of the other conditions which may be responsible. Acute conditions, such as typhoid fever or small-pox, are not considered, as we are dealing only with pain which is of considerable duration.

1. Disease of the nervous system: Meningitis (especially syphilitic), tumors of the meninges, tumors of the cord and cauda equina.

2. Disease of the spine: Spondylitis and perispondylitis, injury, new growth, tuberculosis. Anatomic peculiarities, such as a long transverse process of the last lumbar vertebra.

3. Disease of the muscles and fibrous tissue: Fibrositis, "lumbago."

4. Disease of the pelvic bones.

5. Sacro-iliac joint disease.

6. Disease of the bowel: Carcinoma of the rectum especially.

7. Disease of the urinary tract: Kidney, ureter, bladder, prostate, seminal vesicles, and deep urethra in males.

8. Disease of the pelvic organs in females.

This may seem like a long list, but if each part is studied systematically and also a thorough examination made you will rarely have much difficulty in coming to a conclusion. It is well to exclude any disease of the central nervous system first and then proceed to the study of the spine and the muscles. The sacro-iliac joints and the pelvic bones may be taken next and then the organs in the pelvis. It is possible by a process of exclusion to narrow down the possibilities. The importance of an *x*-ray study is very evident. The chance of there being two lesions must be remembered, sometimes entirely distinct, sometimes associated. Thus a patient may have sacro-iliac joint disease and prostatitis which have no association, or a spondylitis may be secondary to a focus of infection in the prostate.

When the anatomic diagnosis is made an effort should be made to determine the etiology if this is possible. A good example is seen in one of the cases shown, in which a spondylitis was apparently secondary to infection of the tonsils. The patient with a syphilitic spondylitis illustrates the importance of an etiologic diagnosis for proper treatment.

**Treatment.**—The condition which we have been discussing is not a disease, but a symptom. Sometimes we have to be content with treating symptoms, but you will agree that such should not be the case when we can do more. To do that with pain in the lower back demands a diagnosis. When that is determined the treatment must be adapted to what is found. It is usually not difficult to determine what should be done. Your results will be very different—brilliant in some, discouraging in others. But never rest content with anything less than an exact diagnosis if such is possible.

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## CALORIMETRY: ITS APPLICATION IN CLINICAL MEDICINE

### The Value of the Estimation of Basal Metabolism in the Diagnosis and Treatment of Certain Conditions. Illustrative Cases.

To the general practitioner and to us who style ourselves internists "calorimetry" is a vague sort of term. We realize in medicine that it has to do with the measurement of heat given off from the body. Perhaps that is as near to its meaning and value as most of us get.

We are, however, learning that this measurement of heat given off from the body is a clinical method which has become one of the most valuable helps in diagnosis in disturbed function of the thyroid gland, and almost a necessity as a guide to the effect of treatment of such conditions. Besides this inestimable valuable discovery, the use of this laboratory method has been of value in establishing a proper caloric value of diets in typhoid fever; in establishing from a laboratory standpoint the value of fasting in severe diabetes mellitus; in establishing the real value of certain foods, and in fixing the reason for the administration of thyroid preparations in obesity.

We owe our opportunity to make this practical use of calorimetry to a host of laboratory workers, among whom Magnus-Levy, Lusk, Eugene DuBois, Delafield DuBois, Benedict and Means may be said to be leaders, and we perhaps owe its applica-

tion to the diagnosis and guide in treatment of thyroid diseases to Henry Plummer, of the Mayo Clinic.

Calorimetry, or the measurement of heat given off by the body, was originally made of great value by the use of a cabinet, built at great expense (several thousands of dollars), in which the actual amount of heat given off was measured. This is direct calorimetry. Now by the effort of these same laboratory workers the measurement of the heat can be estimated by calculating the gaseous exchange through the lungs, that is, the amount of oxygen consumed, and the amount of $CO_2$ given off in a given period of time. This is indirect calorimetry.

This latter form of estimation is made by the use of an instrument of various types, all, however, having as their basis the amount of oxygen absorbed and the amount of $CO_2$ given off by the lungs.

To understand thoroughly the clinical value of calorimetry we must have a knowledge of the basic principles underlying heat and energy production, whether it be in the human body or the simplest form of combustion such as occurs in a heater.

To produce heat and energy combustion must occur, and to produce combustion fuel is necessary, and to burn fuel oxygen must be consumed and carbon dioxid formed. If we know the amount of oxygen consumed, the carbon dioxid formed, and the type of fuel burned, the heat production can be calculated. In the human being all the oxygen enters through the lungs and the carbon dioxid leaves by the same route, therefore it is that the various types of apparatus employed to determine the heat production are designed wholly to measure quantitatively this gaseous interchange. We also know that fuel used in the human body consists of three kinds of food-stuffs, namely, carbohydrate, fat, and protein, all of known caloric value. From the chemical composition of these foods we can calculate, as will be shown later, the amount of oxygen necessary for the complete oxidation of the substance and the carbon dioxid resulting from this oxidation. These facts can also be acquired by burning a known weight of the food-stuff in a bomb calorimeter, and, in addition, the heat liberated by the combustion can be measured directly.

A study of the relationship between carbon dioxid produced to the oxygen consumed gives us what Pflüger many years ago termed the respiratory quotient:

$$\text{Resp. quotient } \frac{CO_2}{O_2}.$$

Since any volume of oxygen combining with carbon produces an equal volume of carbon dioxid, the ratio $\frac{CO_2}{O_2} = 1$.

Early in the study of calorimetry in the human being it was found that frequently the respiratory quotient was less than 1, depending on the diet.

On investigating the reason for the differing respiratory quotients for each of the three kinds of food-stuffs, using chemical analysis, it was found that when the hydrogen and oxygen of the food-stuff was in the same proportion as water, $H_2O$, the respiratory quotient was 1, as for example, glucose:

$$C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O$$
$$\text{Ratio} = \frac{CO_2}{O_2} = \frac{6CO_2}{6O_2} = 1.00$$

The respiratory quotient for all carbohydrates, including dextrose, levulose, starch, maltose, milk-sugar, is 1.00.

In the oxidation of fat, using tripalmitin as an example, we get the following equation:

$$\begin{array}{rr} & C_{51}\ H_{98}\ O_6 \\ \text{Less the intramolecular water} & H_{12}\ O_6 \\ & \overline{C_{51}\ H_{86}} \end{array}$$

Then, on oxidation,

$$2(C_{51}H_{86}) + 145\ O_2 = 102\ CO_2 + 86\ H_2O$$
$$\text{R. Q. } \frac{CO_2}{O_2} = \frac{102\ CO_2}{145\ O_2} = .703$$

The calculation of the theoretical quotient for protein is complex because the protein molecule is not completely oxidized, a portion being eliminated in the urine as uric acid, urea, creatinin, and the other fractions comprising the total urinary nitrogen.

The respiratory quotient when carbohydrate alone is burned is 1. When protein is burned the quotient is approximately .8, while when fat is burned the quotient is .7.

In severe diabetes when fat alone is being consumed the quotient may be lower than .707, reaching .69.

The importance of the respiratory quotient, clinically, is that it denotes the type of food-stuff being metabolized. If carbohydrate alone is being catabolized a respiratory quotient of 1.00 would result. If the patient is existing entirely on fat, as might occur in starvation, the quotient would be .71. In a normal individual under ordinary conditions the quotient is somewhere between the above figures, depending on the percentage of each of the three food-stuffs comprising the diet. If mostly carbohydrate the quotient would be near 1.00, and near .71 if mostly fat. Under ordinary circumstances a normal individual after fasting twelve to fourteen hours and at rest has a respiratory quotient between .78 and .85, .82 being the average. Protein metabolism plays a small rôle in the total metabolism, averaging about 15 per cent.

Moreover, if we know the amount of nitrogen being eliminated in the urine in a unit of time, *i. e.*, one hour, and the total gas interchange during that hour, we can determine the percentage of fat and carbohydrate burned. It is known that for every gram of nitrogen eliminated in the urine 26.51 calories of heat result, and that 5.91 liters of oxygen are consumed and 4.75 liters of carbon dioxid formed.

If we determine the total gaseous interchange and the total nitrogen output in the urine per unit of time, we can calculate the gaseous interchange for fat and carbohydrate, the so-called non-protein respiratory quotient. The non-protein quotient is the difference between the total gaseous interchange and the oxygen consumed and carbon dioxid eliminated from the metabolism of protein.

After calculating the non-respiratory quotient the percentages of fat and carbohydrate burned can be found by referring to the table of Zuntz and Schumburg.

For routine work protein metabolism can be disregarded, the

total respiratory quotient and non-protein quotient differing so little that they can be considered as the same.

Following the above outline of some of the principles of calorimetry, a discussion of basal metabolism will now be undertaken.

Basal metabolism may be defined as the minimum heat production of an individual, measured after fasting twelve to fourteen hours, and in complete muscular repose for at least thirty minutes before beginning the test. Muscular effort means increased heat production and greater carbon dioxid elimination which upsets, to some extent, the respiratory rhythm.

Starvation is necessary in order to avoid the stimulating affect of food, spoken of as the specific dynamic action of food. The specific dynamic action of food-stuffs is the result of the energy expended by the body in preparing the various nutrients for utilization by the tissues. Digestion and absorption are examples of this. In order for the body to derive 100 calories from the protein eaten, it must expend about 30 calories to prepare the protein for utilization, for every 100 calories of carbohydrates 5 calories are are expended, and about 12 calories for 100 calories of fat.

The other extraneous factors that will increase the basal metabolic rate are shivering, menstruation, fever, psychic influences, such as fear, and certain drugs, such as caffein. Fever increases the metabolic rate considerably because there is a considerable increase in oxidation.

As has been pointed out, the basal metabolic rate may be determined by direct calorimetry or indirect calorimetry. In the former, actual heat production is measured and at the same time the oxygen consumption, carbon dioxid elimination, is determined. The great expense of building and operating this type of apapratus combined with the technical difficulties of operating it, restricts its use to a very few institutions.

The indirect method is the one of especial interest to the medical profession because it is within the reach of the general hospital and physicians both from the standpoint of technic and

financial outlay. The results obtained by the indirect and direct methods check very closely.

In indirect calorimetry we determine the oxygen consumption and the carbon dioxid elimination, and from this study of the gaseous interchange the respiratory quotient is figured. The cal-

CALCULATIONS OF INDIRECT CALORIMETRY

1 gm. urinary N 26.51 calories
1 gm. urinary N 5.91 liters $O_2$ (= 8.45 gms.)
1 gm. urinary N 4.75 liters $CO_2$ ( = 9.35 gms.)
1 gm. $O_2$ = 0.699 liters
1 gm. $CO_2$ = 0.508 liters

The grams of nitrogen of the urine are multiplied by the oxygen and carbon dioxide coefficients. The resulting quantities are deducted from the amounts of carbon dioxide expired and oxygen inspired. The respiratory quotient of these remainders depends upon the relative quantities of carbohydrate and fat oxidized.

| R.Q. | Calories for 1 liter $O_2$ Number | Log. | Carbohydrate per cent | Fat per cent. |
|---|---|---|---|---|
| 0.70 | 4.686 | | 0 | 100. |
| 0.71 | 4.690 | | 1.4 | 98.6 |
| 0.72 | 4.703 | | 4.8 | 95.2 |
| 0.73 | 4.714 | | 8.2 | 91.8 |
| 0.74 | 4.727 | | 11.6 | 88.4 |
| 0.75 | 4.739 | | 15.0 | 85.0 |
| 0.76 | 4.752 | | 18.4 | 81.6 |
| 0.77 | 4.764 | | 21.8 | 78.2 |
| 0.78 | 4.776 | | 25.2 | 74.8 |
| 0.79 | 4.789 | | 28.6 | 71.4 |
| 0.80 | 4.811 | | 32.0 | 68.0 |
| 0.81 | 4.813 | | 35.4 | 64.6 |
| 0.82 | 4.825 | | 38.8 | 61.2 |
| 0.83 | 4.838 | | 42.2 | 57.8 |
| 0.84 | 4.850 | | 45.6 | 54.4 |
| 0.85 | 4.863 | | 49.0 | 51.0 |
| 0.86 | 4.875 | | 52.4 | 47.6 |
| 0.87 | 4.887 | | 55.8 | 44.2 |
| 0.88 | 4.900 | | 59.2 | 40.8 |
| 0.89 | 4.912 | | 62.6 | 37.4 |
| 0.90 | 4.924 | | 66.0 | 34.3 |
| 0.91 | 4.936 | | 69.4 | 30.6 |
| 0.92 | 4.948 | | 72.8 | 27.2 |
| 0.93 | 4.960 | | 76.2 | 23.8 |
| 0.94 | 4.973 | | 79.6 | 20.4 |
| 0.95 | 4.985 | | 83.0 | 17.0 |
| 0.96 | 4.997 | | 86.4 | 13.6 |
| 0.97 | 5.010 | | 89.8 | 10.2 |
| 0.98 | 5.022 | | 93.2 | 6.8 |
| 0.99 | 5.034 | | 96.4 | 3.4 |
| 1.00 | 5.047 | | 100.0 | .0 |

Fig. 102.

culation of the heat produced is determined from the oxygen consumption because it is not as readily affected by alteration in breathing as the carbon dioxid is. Increased rate and depth of breathing means greater carbon dioxid output, while the oxygen consumption is not affected unless the muscles of res-

piration become much more active, which would result in greater oxidation.

Indirect calorimeters can be divided into two types, the Tissot type, in which the patient inspires the air of the room and expires into a gasometer such as is pictured in Fig. 103. The separation of the inspired and expired air is brought about by using a flutter valve. The gasometer is counterpoised so that

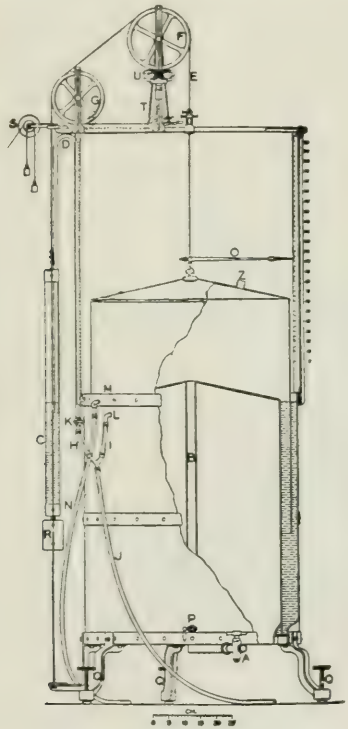

Fig. 103.

there is no increase in pressure. It is also calibrated so the volume of expired air can be measured. An analysis of the air of the room and that in the gasometer is made.

Knowing the volume of expired air, the length of the experiment, and the difference between the oxygen and carbon dioxid contents of the inspired and expired air, the oxygen consumption and carbon dioxid elimination can be calculated.

In the other type of indirect calorimeter the patient breathes into a closed system in which the air is kept constantly circulating through the various absorbants. A counterpoised spirometer maintains a constant pressure and is the means of regulating the amount of oxygen to be added. In this method the expired carbon dioxid is absorbed by soda lime through which the air circulates, while the oxygen is derived from a tank of pure oxygen which is added, as the volume of air in the system de-

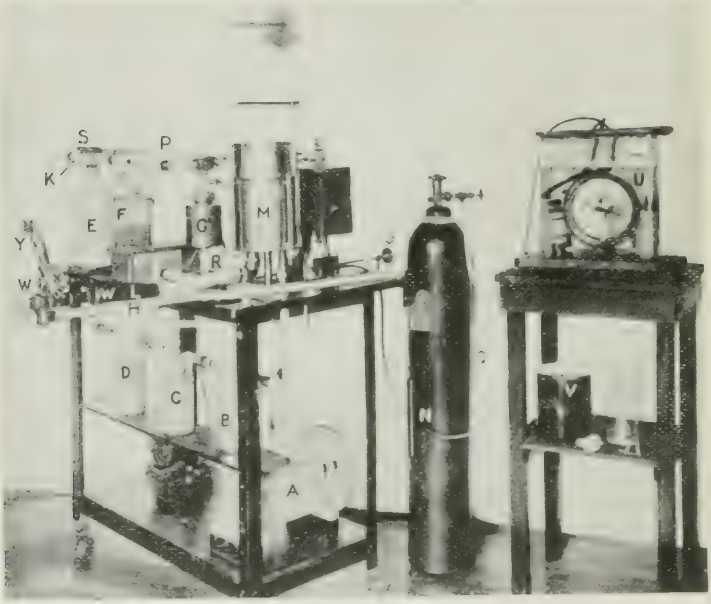


Fig. 104.

creases, so that we always have at the end of the experiment the same amount of air as we had at the beginning.

Carbon dioxid is determined by noting the increase in weight of the vessels containing the carbon dioxid absorbent. The oxygen that enters the system is measured by passing it through a wet gas meter.

This type of apparatus is shown in Fig. 104.

The length of each experiment is from ten to fifteen minutes.

Since human beings vary in height and weight, a definite

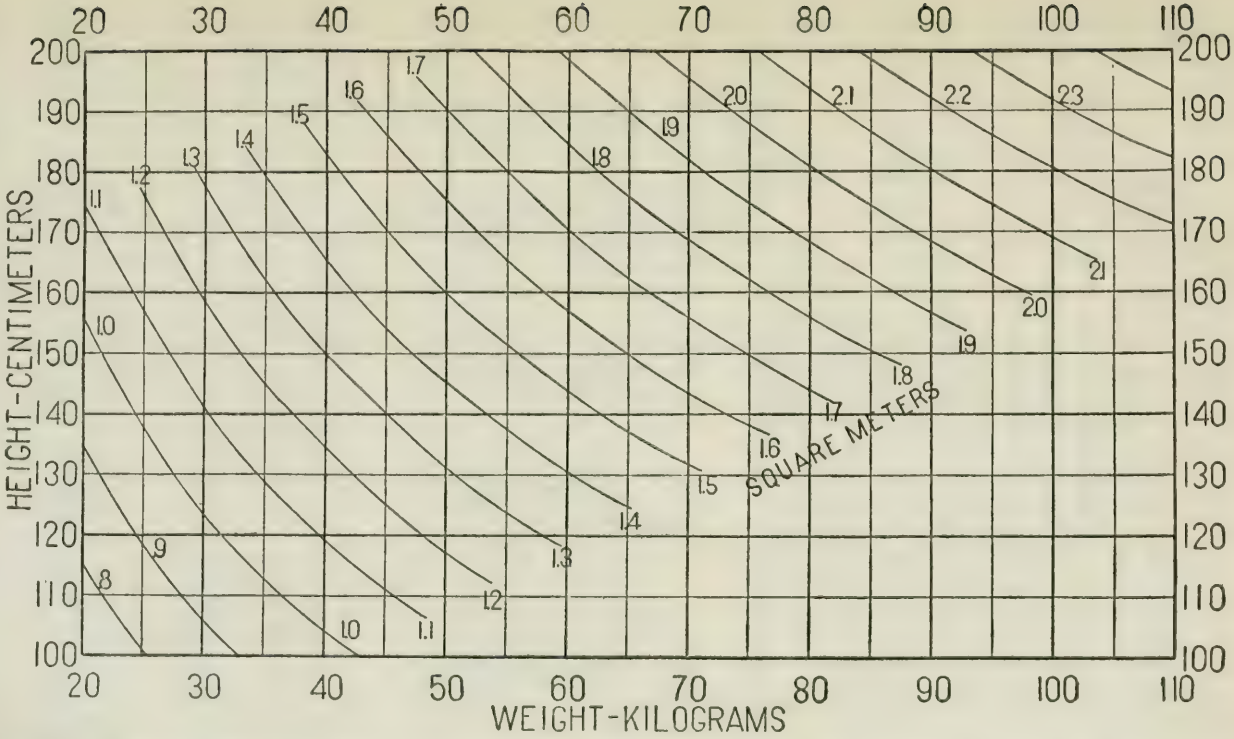


Fig. 105.—Chart for determining area of man in square meters from weight in kilograms (Wt.) and height in centimeters (Ht.) according to the formula: Area (Sq. Cm.) = $Wt.^{0.425} \times Ht.^{0.725} \times 71.84$. (Dubois, D. and E. F.)

method of expressing the results must be used in order to be able to make a comparative study of the results obtained. Since Rubner claimed that heat production is proportional to surface area, the results are expressed in calories per square meter of the body surface per hour. Dubois has worked out a formula whereby the surface area can be calculated very accurately if one knows the height and weight of the patient. From this formula,

$$\text{Wt.}^{0.425} \times \text{Ht.}^{0.725} \times 71.84 \text{ (71.84 is a constant)}$$

he has derived the chart shown below which simplifies the calculation of surface area very materially.

Standards of Normal Metabolism
Average Calories Per Hour Per Square Meter of Body Surface (Du Bois).

| Age (Years) | Males Cals. | Log Cals. | Females Cals. | Log Cals. |
|---|---|---|---|---|
| 14-16 | 46.0 | 1.6628 | 43.0 | 1.6335 |
| 16-18 | 43.0 | 6335 | 40.0 | 6021 |
| 18-20 | 41.0 | 6128 | 38.0 | 5798 |
| 20-30 | 39.5 | 5966 | 37.0 | 5682 |
| 30-40 | 39.5 | 5966 | 36.5 | 5623 |
| 40-50 | 38.5 | 5855 | 36.0 | 5563 |
| 50-60 | 37.5 | 5740 | 35.0 | 5441 |
| 60-70 | 36.5 | 5623 | 34.0 | 5315 |
| 70-80 | 35.5 | 5502 | 33.0 | 5185 |

Fig. 106.

Heat production varies with age and sex, as is shown in Fig. 106. This table shows the average normal for various ages in both sexes. A variation of ± 10 per cent. from the figure in the table is considered normal and nothing abnormal unless greater than 15 per cent.

This chart is correct to 1.5 per cent. for all sizes and shapes of the human body.

My purpose in bringing this subject before you is to persuade you, as I have been shown by instruction and experience, that the estimation of this basal metabolism is of greatest value in the diagnosis and treatment of certain conditions, particularly diseases of the thyroid gland.

Its value in the establishment of a diet in typhoid fever was shown by Coleman and DuBois, Archives of Internal Medicine, Vol. 15, 1915, page 885. They showed that proteins, carbohydrates, and fats were oxidized during an attack of typhoid fever in exactly the same manner and just as efficiently as in health. They also proved that a higher caloric value of food is important in typhoid fever patients, because the basal metabolism is greater than in health, thus proving by experimental means the truth long taught by some clinicians that all forms of food can be burned by the fever patient. Certain clinicians

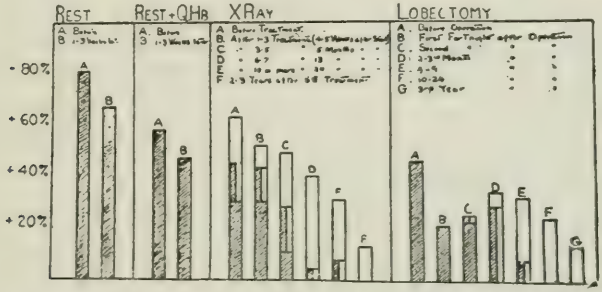


Fig. 107.—Diagram showing average metabolism levels and effect of various sorts of treatment thereon. The columns indicate the percentile increase above the standard. The shading indicates what proportion of the patients forming any average were receiving complete rest (full shading), partial rest (half-shading), and what proportion were leading their usual lives (unshaded).

claimed this, and gave their patients an abundance of all sorts of food provided it was a form which would not irritate the diseased and often ulcerated intestinal tract.

Allen and DuBois (Archives of Internal Medicine, 1916, Vol. 17, page 1010) studied 3 very severe diabetics and compared them with 3 normal individuals.

In these experiments the observers seem to have established that the oatmeal cure of the von Noorden School has no especial influence on the treatment of diabetes, and perhaps drives home the fact that the oatmeal cure in diabetes is not in any sense the valuable asset the average physician believes it to be.

The experiments also give no grounds for the belief that glucose is formed from fat.

By the use of the calorimeter in these experiments it was proved that patients with diabetes mellitus as a result of fasting can utilize carbohydrates derived from their own body protein, and later from the protein and carbohydrate of a carefully regulated diet.

Still another important clinical fact which seems to be established (Means, Jour. Med. Research, 1915, Vol. 32) is that in obesity there is no evidence that the administration of thyroid preparations causes destruction of body fat, but by causing a better utilization of carbohydrates it may prevent or lessen the formation of fat from carbohydrates and thus lead to a better dietetic treatment, and in a later communication (Archives of Internal Medicine, 1915, Vol. 17, Part I) Means concludes from the study of 8 cases of adiposity that there is no increase of metabolism in these fat individuals.

In cardiorenal cases Peabody, Meyer, and DuBois (Archives of Internal Medicine, Vol. 17, Part I, 1915, p. 980) show that the basal metabolism is distinctly raised in non-compensated cases, while in compensated cases the metabolism is at a normal rate.

The above observations are all valuable and add much to the diagnosis and treatment of these conditions, but are relatively insignificant when compared to the value of metabolism estimates in the diagnosis and treatment of diseases of the thyroid gland.

First, in hypothyroidism the question of diagnosis is very frequently difficult and uncertain, particularly in myxedema occurring in adults.

The deterioration mentally, the change of the hair, the thick dry skin are suspicious of lack of function of the thyroid gland, but these symptoms occur in other conditions. In hypothyroidism, however, there is marked lowering of basal metabolism which does not occur in other conditions with similar symptoms. If there is a lowering of basal metabolism in these suspicious cases it proves the case of thyroid origin, and we can administer desiccated thyroid with assurance that it will prove a specific.

Not only is the metabolism estimate of value in making

certain diagnosis, but by it one can control the amount of desiccated thyroid to be used. In a case of my own—

Mrs. W. P., aged fifty-two. First seen April 21, 1918. Her chief complaint was numbness in her hands and feet, hands and face swollen, cold hands, considerable headache. Marked gain in weight. Thirty years ago she weighed 115 pounds, now weighs 165, two years ago 153 pounds. She has been under considerable strain for the past five years. Has a good appetite, eats considerable food, no dyspnea, some palpitation of heart, some looseness of bowels, is getting dull, and seems to be losing her senses. Her face is round, the skin is thick and swollen. However, the skin, which looks swollen, proves, on palpation, not to be edematous. The lips are dry, the skin of the legs and face is scaly, the skin of the back is so thick it cannot be pinched up, the hair is soft. Thyroid gland could not be felt. There was a prompt patellar reflex. Her pulse was 68 and full, there was no abnormality of the lungs. She was thought to have hypothyroidism, and was at once, without the metabolism test being taken, put upon desiccated thyroid gland. In twenty-three days her metabolism was taken, and found, according to Dr. Jonas, to be 20 per cent. above normal. She was very rapidly losing weight, and this, together with her high metabolism instead of low, caused us to lower the dose of desiccated thyroid to 1 grain. She made a complete recovery, and today she is still taking her thyroid extract and has no signs of hypothyroidism.

**Hyperthyroidism.**—All who have to do with patients can make a diagnosis of Graves' disease when the patient is tremulous, has a large pulsating thyroid, has persistent tachycardia, has prominent, staring eyes—and we do not *need* an estimation of metabolism to make a diagnosis. In the border-line cases, however, where there is a large goiter or no marked thyroid enlargement, where there are no eye symptoms, where there is intermittent though perhaps not continuously rapid heart, where there is much "nervousness" and often tremor, the estimation of basal metabolism makes the diagnosis and treatment at once certain.

Mrs. L., aged fifty-two. Has been complaining for two

years of severe headaches, which come on during her menstrual period. They come on suddenly, no vomiting, has had considerable palpitation of her heart, worse lately. Developed a goiter several years ago and with it noted palpitation of the heart. She has lost some weight lately, but is gaining again. Gets attacks of severe diarrhea. She notices a tremor of her hands. She sweats very easily, her face flushes, she gets attacks of vertigo. There was a moderate enlargement of the thyroid gland. A very distinct erythema follows a finger scrape. Auscultation of thyroid gland does not show any undue pulsation, no thrill. There is marked tremor of her hands, she is easily disturbed mentally, her pulse-rate averages 100. There is no organic disease of the heart. Blood-pressure 200 systolic and 110 diastolic. Urine was normal. She showed considerable anemia, 75 per cent. hemoglobin, 3,700,000 red cells. As will be seen, the symptoms described might make the case easily mistaken for hyperthyroidism. She was sent for metabolism test and, according to Dr. Jonas, her metabolism was entirely within normal limits. This allowed us to make a positive diagnosis of a neurasthenic condition probably accompanying the menopause, and her thyroid, which was large, had nothing to do with her condition. She was treated accordingly, and the progress of the case showed that she never did have hyperthyroidism.

A very similar case was seen on October 4, 1920.

Patient aged thirty-eight. About one year ago she noticed that her pulse was fast, that she was short of breath, had a pain around her heart. Pain was constantly present and more severe on exertion. She had considerable tremor of both fingers and hands when the arm was extended. Pupils reacted to light, no eye symptoms of hyperthyroidism, the patient was obsessed with the thought, however, that she had hyperthyroidism. She was sent for metabolism test, and Dr. Jonas reported that the metabolism was 3.8 per cent. *below* normal, marking the case certainly as one of neurasthenia.

Mrs. C. was seen in August and September, 1920. She had the history of an operation, removal of one kidney about three years ago. Since that she had entirely recovered.

In July, 1920 it was discovered that she was getting weak, could stand no exertion, that her heart was very rapid, and that she had a slight enlargement of her thyroid. Her physician considered that she probably had hyperthyroidism. She was seen, found to be slightly anemic, her urine was normal, she had marked tremor of her hands, she had a slightly enlarged thyroid, and her pulse averaged about 120 to the minute. She also was sent for metabolism test, and found to have a rise of 19 per cent. above normal. She was given *x*-ray treatment. Three weeks after that she came back and was found to have 45 per cent. rise, notwithstanding the fact that she was considerably better. She had gained 3 pounds in weight, did not complain of her palpitation, and felt stronger. This rise in metabolism after *x*-ray treatment of her thyroid is difficult to account for. It may be possible that at the last examination there was some undue excitement or she had taken some undue exercise, although all care was taken. She had been in bed twelve hours before the metabolism test was taken the last time.

Mrs. C.'s case has bothered me for months until the basal metabolism as estimated by Dr. Jonas proved it to be 17 per cent. above normal. She is a woman aged forty-six, in very moderate circumstances. She has had rapid heart beating, some tremor, no enlarged thyroid, eyes slightly prominent, but without any of the typic signs of exophthalmos. She is thin, expresses herself as extremely nervous, and her one complaint in addition to this is her rapid heart. I believe this case also to be one of mild hyperthyroidism.

All men who have made use of this test are of one mind as to its absolute diagnostic value. Cases of effort syndrome can be separated from possible hyperthyroidism; cases of mild tuberculosis with tachycardia and neurasthenic symptoms can be separated from hyperthyroidism.

All of us have hesitated when in the presence of severe cases of Graves' disease as to the time of operation. It is now an accepted axiom that cases with a very high metabolism are very bad surgical risks and such cases must be given the benefit of rest, and perhaps *x*-ray, before they are treated surgically.

Again, the cure of the disease under *x*-ray treatment can be gaged by metabolism estimation. However, there is some uncertainity as to the exact interpretation in such cases as shown by Mrs. C. just quoted. Her metabolism was 19 per cent. above normal on the first estimation. The second estimation three weeks later after being treated with *x*-ray by Dr. Pancoast was 45 per cent. above normal. I am at a loss to explain this because the patient has gained 3 pounds and is symptomatically better. Many articles are published regarding the value of diagnosis and effect of treatment of basal metabolism estimates.

As to the relative value of treatment by *x*-ray and surgery of hyperthyroid cases: Means published (Archives of Internal Medicine, 1919, Vol. 24. No. 6, pages 645–677) a study of 130 cases in which 345 metabolism estimates were made over a period of years. He compares treatment by rest, by hydrobromate of quinin alone and combined rest, by *x*-ray, and by surgery.

In making estimates 10 per cent. above and below were disregarded. Rest alone caused a certain drop and sometimes a permanent cure.

Hydrobromate o quinin combined with rest is not superior to rest alone.

*x*-Ray causes a gradual fall of metabolism. Surgery causes a rapid fall of metabolism, then a secondary rise, with a final fall.

This does not necessarily mean that *x*-ray is a superior treatment to surgery, but it certainly proves that it is a valuable treatment, and may be used in severe cases where surgery may be dangerous as an adjunct to surgery, or light cases, or cases which refuse surgery.

My plea is to all of you to make use of this most valuable diagnostic method. Make use of it by urging each of your local hospitals to install an instrument to be operated by someone who has the knowledge to operate it accurately.

It is neither practicable nor desirable that the practising physician attempt to do the work. It is difficult, time-consuming work, taking a skilled operator, but it pays to have the work done by someone who is convenient with your work, because your diagnoses will be accurate and your treatment better controlled.

## CLINIC OF DR. DAVID RIESMAN

PHILADELPHIA GENERAL HOSPITAL

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### PHLEBITIS AND THROMBOSIS

THE patient I show you today is John Wallace, thirty-seven years of age, who has had lobar pneumonia. He is an old alcoholic and was desperately ill. In the beginning the left apex was alone involved, but the inflammation extended down to the lower lobe, the process fortunately remaining confined to the left side. We were doubtful as to the man's recovery, but nature came to our aid and he did not die. His is one of the cases that proves that the so-called Gibson rule, according to which, when the blood-pressure in falling crosses the pulse-rate a fatal termination will occur, is not always true. At one time his systolic blood-pressure was 100 and the pulse 125. As the urine contained a considerable amount of albumin and granular casts we had an added reason to feel that the outlook was dubious. However, he got well, was up and about a few days, and was ready to receive his discharge, a wiser and better man, when be began to complain of severe pain in the left calf and limped a little about the ward. The pain and difficulty in walking rapidly got worse, he suffered a great deal, and the limb began to swell. We have figured out that this particular complication involving the left leg, on account of which I am bringing him before you, began two weeks after the crisis.

What has happened in this man? What do the students think? Yes, a phlebitis. You can readily see the difference in the size of the two limbs; that the left is much the larger; it is very tense and tender; you note he winces when I touch the skin.

Phlebitis as a pathologic process is closely related to thrombosis. I need scarcely rehearse to you the much-discussed subject of blood-clotting which underlies thrombus formation. You know there are two principal theories—that of Morawitz and

that of Howell. Both theories are in agreement as to the source of fibrin—that it is derived from fibrinogen through the action of thrombin. The points in dispute, as stated by Macleod (Physiology and Biochemistry in Modern Medicine, St. Louis, 1919, p. 106), concern the origin of the thrombin and the mode of action of the calcium ion and the thromboplastic substances. According to Morawitz, the thrombin exists in living blood in an inactive state called thrombogen (prothrombin), which becomes converted into thrombin by the simultaneous action on it of soluble calcium salts and of thromboplastic substances furnished by the tissue cells in general and by the cellular elements of the blood-platelets and leukocytes. According to this view the thromboplastic (prothrombin) substance, aided by the presence of calcium ions, converts thrombogen to thrombin. It acts, therefore, as a kinase and is called thrombokinase. The fundamental fact of this theory, then, is that kinase is necessary for the union of the calcium with prothrombin—a fact, however, which is challenged by Howell, who states that prothrombin may be converted to thrombin by the action of calcium ions alone. This investigator believes that the thromboplastic substance acts not as a kinase, but because it neutralizes antithrombin, which is constantly present in the blood, and the function of which is to prevent the calcium from uniting with the prothrombin to form thrombin. Howell's theory in his own words is as follows: "In the circulating blood we find as constant constituents fibrinogen, prothrombin, calcium salts, and antithrombin. The last-named substance holds the prothrombin in combination and thus prevents its conversion or activation to thrombin. When the blood is shed the disintegration of the corpuscles (platelets) furnishes material (thromboplastin) which combines with the antithrombin and at the same time liberates more prothrombin; the latter is then activated by the calcium and acts on the fibrinogen." Antithrombin can also prevent the action of thrombin on fibrinogen.

Thrombosis is usually defined as the clotting of the blood during life in the heart or vessels. That is not strictly correct. The product is not always a clot, according to recent researches,

but often merely an agglutination which does not show all the elements of a true clot, so that many define it now as a form of plug or mass in the heart or vessels derived from the constituents of the blood (Welch). These clots may form in the heart, in the arteries, in the veins, and in the capillaries. In the heart the clots are seen constantly at autopsy and are nearly always of postmortem origin. Nevertheless, clots may form in the heart during life under several conditions. Although heart-clot is often assigned as the cause of sudden death in diphtheria, pneumonia, and typhoid fever, this is rarely correct. Antemortem clots are found in cases of marked weakness of the heart muscle; they are particularly common in mitral stenosis. In that disease one finds clots of various shapes in the left auricle, pediculated and ball thrombi, and adherent or parietal thrombi.

In the arteries thrombosis occurs under a variety of conditions. Ligating a vessel produces a clot. In aneurysm clots form and may bring about healing; in arteriosclerosis clots are often deposited within atheromatous vessels, especially in the coronary and cerebral arteries.

The veins are the seat, par excellence, of thrombosis; any vein may be affected. In our patient, Wallace, it is the veins of the lower extremity; in that respect his case obeys the rule, even in the side affected, for the largest number occur in the left leg. I shall not go into the reasons, which are largely anatomic, for this preference. Other situations of thrombosis are the mesenteric veins, the inferior vena cava, and the cerebral sinuses, etc. Thrombosis of the cerebral sinuses is rather important; I will touch upon it later. Thrombosis finally is common in the hemorrhoidal veins.

**Capillary thrombosis** is usually an agglutinative process, so-called hyaline thrombosis. Hyaline thrombi have attracted a good deal of attention among pathologists; clinically, we cannot make use of the knowledge so far developed. So much for the seats of thrombosis.

The majority of cases of thrombosis in the veins seen clinically are real forms of thrombophlebitis and are due to infection, either with the organism of a primary disease or with a secondary

invader. Virchow established the class of so-called marantic thrombi which are supposed to be due to a stagnating circulation. The peculiar behavior of these types of thrombosis, which I have seen especially in decompensated heart disease and in advanced pulmonary tuberculosis, makes me feel that there, too, a low-grade infection is at work.

A few words about the **clinical causes:** Judging from my own experience, the majority of cases I have seen have followed typhoid fever; obstetricians see it most often after labor. Phlebitis is common in typhoid fever. When I say "common" it is a relative term; it occurs in 2.5 per cent. of cases of typhoid fever, using large statistics as a basis, and is in typhoid fever nearly always a venous process—a thrombophlebitis; it occurs usually in the leg, before the patient leaves his bed, and is frequently overlooked. The patient complains perhaps of a little pain in the leg; the doctor does not pay attention to it until he or the nurse notices that the temperature and pulse are rising, and the patient is not doing so well as before. If a blood count is made, an increase of leukocytes will nearly always be found. Last year we had a patient in Ward 14 whose case is worthy of brief mention here: The man and two children were in the Philadelphia General Hospital; his wife was in the Polyclinic Hospital; all were suffering from typhoid fever. The man was quite ill, had the characteristic symptoms of typhoid fever, but failed at all times to give a positive Widal reaction. After tedious convalescence we allowed him to get up. Within a few days he was seized with a violent pain in the left inguinal region radiating into the left leg. There was persistent pain and tenderness above the groin, but neither swelling nor tenderness in the leg. The leukocytes, which had been low, rose to about 13,000, and the fever returned. There was no evidence of perforation, and after eliminating the various possibilities we could think of, we decided there was a thrombosis of the deep pelvic veins. The man made a complete recovery. It was of great interest to us to find that during this episode the Widal reaction for the first time became positive.

A few years ago Dr. L. A. Conner, of New York, made a valuable contribution to the subject of thrombosis in typhoid

fever by pointing out that phlebitis was not limited to the large veins of the leg. He showed quite convincingly that there was a phlebitis in the small veins of the feet which readily explained the "tender toes" of typhoid fever—a common and distressing symptom formerly looked upon as a so-called end-neuritis. Conner also suggested that some of the pulmonary symptoms of typhoid fever, such as sudden pain in the chest suggesting a small patch of pleurisy, might be dependent upon the same process in the pulmonary veins, a localized thrombosis. Thus the thrombotic process may have wide distribution in typhoid fever, perhaps also in other diseases. I may add that chills in typhoid fever, often mysterious and difficult to account for, may be due to deep-seated thrombophlebitis.

**Pneumonia.**—Thrombophlebitis in pneumonia, as found by the patient I have just shown you, is not common according to statistics; yet I have seen a number of cases myself. All of my patients that have had it have gotten well. Whether one could conclude from this that it is a favorable prognostic element I am not prepared to say. As the worst is usually over when phlebitis sets in, it does not affect the outcome unfavorably.

**Influenza.**—Thrombosis is fairly common in influenza, causing the same acutely painful swelling that occurs in pneumonia and typhoid fever. Frequently, however, the process affects the arteries and leads to gangrene.

**Tuberculosis.**—I have seen a few instances of thrombosis in tuberculosis. It occurs both in the legs and in the arms. In this disease it has, I believe, a very unfavorable significance, and in that respect affords a guide to prognosis which, as you know, is proverbially difficult in consumption. I have found that after thrombosis occurred in a case of pulmonary tuberculosis life was usually a question of not more than six weeks or two months. The thrombosis is probably not a tuberculous process, but is due to circulatory weakness, to changes in the composition of the blood, and probably, as already mentioned, to a low-grade secondary infection.

**Chlorosis.**—Thrombosis occurs in about 1 per cent. of cases of chlorosis, but among this 1 per cent. the distribution is interesting

Of 86 cases collected by Welch, 48 were in the legs and 29 in the cerebral sinuses. There is no satisfactory explanation for the thrombosis in chlorosis.

**Thrombosis in Heart Disease.**—I have already spoken of intracardiac thrombi, and now I want to say a word about peripheral thrombosis. We have recently had in the wards of the Philadelphia General Hospital two large negro women suffering from myocarditis with dilatation of the heart. The thrombosis affected in one case the axillary vein; in the other the axillary and cervical veins. The left arm in both was enormously swollen and painful; in one there was also a brawny swelling of the neck. At first it looked as if the condition was a cellulitis, but we were finally convinced that it started as a thrombosis in the veins.

**Pulmonary thrombosis in heart disease** should be mentioned at this point. In mitral stenosis—less often in regurgitation—also in myocardial disease without valvular defect, patients may have attacks of blood-spitting, sometimes with sharp, localized pain in the chest. This condition is usually ascribed to congestion of the lungs; in mitral stenosis it is sometimes mistaken for pulmonary tuberculosis. The true cause is probably areas of infarction, the result of thrombosis. Similar symptoms may be produced by small emboli leading, as do thrombi, to areas of hemorrhagic infarction.

**Puerperal thrombosis,** also known as **phlegmasia alba dolens,** is a well-known complication of the puerperal state, usually unilateral, and unquestionably due to infection of a mild character. Many women that have had phlegmasia are left, like Mrs. Belkowitz, in Zangwill's Children of the Ghetto, with one thick leg and one thin one.

A condition comparable to phlegmasia alba dolens occurred some time ago in a man in Ward 13, about whom we had a good deal of discussion. He had general peritonitis. Suddenly he was seized with a frightful pain in the left leg which swelled up to great size. There was no pulse in the femoral artery or any other artery accessible to touch in the leg. The skin was tense and glazed. Some thought the obstruction arterial, but on

account of the great swelling and general resemblance to phlegmasia I was inclined to the diagnosis of thrombophlebitis. The autopsy showed a clot in the veins and nothing in the arteries.

**Postoperative Thrombosis.**—In a sense this is a natural result of the ligation of severed vessels. It may, however, occur in veins that are not cut, but that have been subjected to rough handling. If it goes beyond the local needs of the operative trauma, it may become a serious danger involving the possibility of embolism. This dangerous accident occurs, as a rule, late—ten days to two weeks after the operation—and follows most often after abdominal operations. Some believe that it is due to the use of large retractors which pull on the edge of the wound and cause injury to the veins, especially the deep epigastric. It is from such veins that emboli are broken off and are swept into the lung where their lodgment usually causes death with terrifying suddenness. Such a tragic accident may occur after a simple appendectomy or other abdominal operations and even after trivial pelvic operations.

Phlebitis may follow prostatectomy, though it is infrequent, and usually occurs in the leg (Crenshaw, Collected Papers of the Mayo Clinic, VIII, 1916, p. 446). Attempts have been made (Bumpus, Ibid.,Vol, IX. 1917, p. 229) to prevent the complication by the use of vaccines. Results, however, have not been satisfactory.

Thrombosis of certain special venous territories is an interesting subject. First of all, thrombosis of the splenic and portal veins. Sometimes this is due, especially portal thrombosis, to the ingrowth of a malignant tumor into the portal vein. It is signalized by a rapidly forming ascites and characteristic engorgement of the cutaneous veins. Varying degrees of thrombosis in the splenic vein may occur in splenomegaly and especially in splenic anemia. As Balfour (Collected Papers of the Mayo Clinics, IX, 1917, p. 321) remarks, this finding suggests that the condition is an etiologic factor in certain cases of splenomegaly and that thrombophlebitis of the splenic and portal veins occurs as a primary condition, that it is a clinical entity and is associated with a rather definite clinical picture in which

enlargement of both spleen and liver, ascites, epigastric pain, and possibly a history of traumatism are features. Rolleston has suggested splenectomy for this condition.

A word more about portal thrombosis. Sometimes after a hemorrhoidal or appendix operation signs of severe septicemia or pyemia make their appearance due to a thrombophlebitis of the portal veins, the so-called pylephlebitis, which is usually attended with the formation of multiple abscesses in the liver.

I do not mean to say that septicemia following an appendicitis operation is necessarily due to a pylephlebitis; a similar clinical picture may be produced by subdiaphragmatic abscess.

**Thrombosis of the inferior vena cava** is most commonly due to tumor metastasis. It may be suspected when in a case of carcinoma of the liver, for example, there is a rapid swelling of the legs with ascites.

**Mesenteric thrombosis** is an interesting condition, and as it is amenable to surgical treatment its timely recognition is important, though rarely accomplished. The symptoms resemble those of acute intestinal obstruction with pain, distention, bloody stools, and signs of collapse. Block and Goldberg have recently reported a case of mesenteric thrombosis successfully operated upon by a complete resection of the intestine.

There is another condition related to the general subject of thrombosis that merits brief consideration. Occasionally young persons between twenty and forty years develop gangrene of the lower extremities. A great many years ago I saw a man thirty-four years old, who was my first case of this kind. He had intense pain in the toes of one foot. Various diagnoses were made; it was before Dr. Leo Buerger, of New York, wrote his classical papers. An ulcer appeared upon the toe and would not heal. The pain was so severe that morphin did not control it; nothing helped the poor fellow. Finally a patch of gangrene became manifest on the toe and the surgeon cut the toe off. Had we known what we learned later, we should not have been content with that operation. For two or three days the man was better, then the pain came back just as severe as it had been. The same surgeon then resected the nerves—the musculo-

cutaneous, the anterior tibial, etc.—cutting out a good-sized piece of each. When the man came out of ether he felt relieved, but in a day or two the trouble recurred; so we next cut off the foot, but without better result. There was then nothing left to do but to cut off the leg below the knee. To our dismay the process then started on the other side. We at once amputated high up near the knee, which gave the patient relief. As so often happens in practice, while attending this man I saw a second case, a small merchant in Camden, thirty-eight years old. Both patients were Russian Jews, an important point since the condition has been found most common in members of that race.[1] Aside from the racial factor tobacco plays a very important rôle.

The disease of which these two patients are examples was formerly called endarteritis obliterans, but according to Buerger it affects both arteries and veins, and is therefore more properly designated thrombo-angiitis obliterans. Buerger's studies on this subject have been so epoch-making that he deserves the honor of having the disease named for him.

Barcroft and other English physiologists have shown the fundamental importance of oxygen for the life of tissues. May not in Buerger's disease a lack of oxygen be as important an element in the devitalization as the lack of the non-gaseous constituents of the blood?

The characteristic features of Buerger's disease are pain, discoloration, and redness when the foot is held down and pallor when it is lifted up; paresthesia, blebs, ulcers, and gangrene. Examination of the arteries in the early stages shows obliteration of the pulse in the dorsalis pedis, often also in the posterior tibial. Sometimes in association with these symptoms migrating thrombosis in the superficial veins of the legs occurs, and as this may appear early it permits of an earlier diagnosis of the under-

[1] At the present time there is in the wards of the Philadelphia General Hospital a Lithuanian, thirty-seven years old, an employee of the Pennsylvania Salt Works, who has gangrene of the foot due apparently to arterial obstruction. This man is not a Jew, but belongs to that mysterious ethnic group which some anthropologists consider the survivors of the primitive Aryans in Europe.

lying condition. In rare instances the thrombus or thrombi become channeled or retracted with the re-establishment of the circulation.

I shall not go into the subject of the treatment of Buerger's disease. I will merely say that in order to avoid amputation attempts have been made to re-establish the circulation by anastomosis of vessels high up in the leg, and also by the intravenous injection of solutions of sodium citrate; the latter has been successfully accomplished in a number of cases by Dr. W. A. Steel, of this city. Dr. Willy Meyer (Jour. Amer. Med. Assoc., April 3, 1920), who has had a large experience in thromboangiitis obliterans, feeling that hereditary influence, nervous instability, and tobacco are important factors in its production, advocates prophylactic instruction.

**Spontaneous Thrombosis in the Legs.**—Sometimes apparently healthy persons are seized with violent pain in the leg as if a blow had been struck against the leg. In one case related by Dr. Coplin, of the Jefferson Medical College, a man walking in Fairmount Park suddenly experienced a violent pain in the calf of his leg. Believing that someone had hit him with a stone, he turned around prepared to strike his assailant, only to find no one in sight. A relative of mine while climbing one of the mountains of the Swiss Alps was suddenly seized with such great pain in the lower leg that he had to break the trip and return to his hotel. A local doctor told him he had ruptured the tendo achillis and bandaged the ankle. When I saw him a few days later in Paris the leg was swollen and tender along the posterior aspect, giving all the signs of a deep-seated thrombosis in the veins of the calf. A rubber stocking helped him greatly. He has had several recurrences of the condition, and is forced to wear a support almost constantly. His general health is excellent.

**Migrating Thrombosis.**—This interesting condition, on which Dr. John Phillips, of Cleveland, has written a valuable essay, is but poorly understood. It occurs in the form of acutely inflamed reddish or purplish, tender, indurated masses usually on the lower limbs. The areas are larger than those of erythema nodosum and

resemble erysipelas or cellulitis. To all intents and purposes they are patches of cellullitis starting as a thrombophlebitis. They have a tendency to recur again and again. Local foci of infection should be searched for in the tonsils, teeth, etc., though they are rarely found. The Wassermann test for syphilis is also desirable. Some writers attribute the condition to gout, but gout is a tolerant disease and is made responsible for many obscure conditions that in their final analysis have nothing to do with it.

**Treatment of Thrombophlebitis.**—I shall deal chiefly with the type occurring in infectious diseases—pneumonia, typhoid fever, etc., and the spontaneous thrombosis discussed on page 1014. What I have to say, of course, applies to puerperal and post-operative thrombosis as well. The first essential is to avoid all unnecessary handling; all rubbing or massage. The limb must be kept at rest, elevated on a pillow, and wrapped in lamb's wool or cotton batting, held on with a loose bandage. The limb should be protected from the weight of the covers by a so-called cradle which is easily made from a barrel-hoop. A pad should be kept under the heel. If the pain is severe, lead-water and laudanum, saturated solution of magnesium sulphate, or kaolin paste should be applied; it may be necessary to give morphin. The bowels must be kept open and the treatment required for the general condition carried out.

Ribbert, a noted pathologist, believes that thrombophlebitis may be benefited by the anticoagulant sodium citrate. The dose is 1 to 2 grams three times a day. As in medical cases one cannot foretell the on-coming of the condition, the use of the drug is hardly practical, although if there is evidence of extension of an existing process, it may be entirely proper to employ it. Chantemesse recommends the use of from 15 to 18 grams of citric acid for two or three days before operations to prevent postoperative thrombosis.

After the acute symptoms are over the patient should wear an elastic bandage, preferably of cotton, or a rubber or laced stocking. Massage is contraindicated, as I have said, in the early stages, but later it may be of benefit.

## CLINIC OF DR. JOSEPH SAILER

PHILADELPHIA GENERAL HOSPITAL

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### A CASE OF PERNICIOUS ANEMIA

PERNICIOUS anemia is sufficiently common in our wards to require some unusual features in a case to justify its presentation. These features in the present case are:

1. A severe type of pernicious anemia followed by a remission.
2. Progressive nervous disturbances increasing during the early period of the remission and then apparently remaining stationary.
3. A pronounced ruddy color of the skin during the remission, notwithstanding there is still a moderate anemia.
4. The presence of the female type of mammary glands with large nipples.
5. The employment of various forms of treatment and consideration of their effects, if any.

W. F.'s family history is unimportant. In the winter of 1917–18 he noticed shortness of breath and felt weak, but improved in the spring. He was not obliged to stop working, but in the fall of 1918 he became worse again, and stopped work some time before Christmas. At this time people remarked to him upon his peculiar color. He states that he had lost 10 pounds in weight during the year 1918. He entered the hospital March 4, 1919. The notes on admission are as follows:

Well-nourished white male, apparently older than his age. The skin is of the characteristic lemon yellow, the lips and mucous membranes almost white. The hair is gray, but fairly abundant. The ears and eyes are normal. The teeth are carious, some snags remain, and the gums apparently are infected. The lungs are normal. The heart is not enlarged to percussion, but a soft systolic murmur can be heard at the apex. The sounds are of moderate intensity. Both the liver and spleen are palpable

below the costal margin. There is also a note that the knee-jerks are decreased, but I feel that this is doubtful.

On March 16th he had a small hemorrhage from the nose.

An April 18th Dr. George Wilson made the following report on the condition of the legs: "The patellar and Achilles' tendon reflexes are present and above normal. When the patient was admitted the plantar reflexes were distinctly normal in type. For the last week this reflex on the left has been undergoing a change, sometimes there is an extension response, which is not, however, a typical Babinski. The sense of position is not disturbed, the patient calls correctly every position into which his toes, ankles, knees, and hips are placed. The other forms of sensation which are carried by the columns of Goll and Burdach, *i. e.*, the sense of vibration is lost as high as the patella on the left and 2 inches above the patella on the right."

The interesting features of this report are, first, the evidence of progressive morbid changes in the findings; second, the change in the left plantar reflex; and third, the loss of vibratory sense, perhaps the earliest definite disturbance of sensation that occurs in lesions of the posterior columns of the cord. Evidently we were observing the earliest recognizable stage of the lesions of the spinal cord in pernicious anemia.

An attempt was then made to eliminate possible causes. An *x*-ray of the teeth had shown pus-pockets at the apices of the teeth. The coagulation time of the blood was tested and found to be normal, and the dentist of the hospital requested to operate, and on May 30th he extracted under local anesthesia two teeth and the roots of two teeth that had been broken off.

It is to be remarked of the table on page 1019 that in the beginning the red blood-cell counts were made with great care, usually by two or more men, and that an even lower count (78,000) than any recorded, is said to have been made by eight men. The hemoglobin estimations were made by the Dare hemoglobinometer, and as this instrument requires some technical skill, and the readings were made by a number of persons, the results are probably not all accurate. The color index is, therefore, of no worth except that it is above normal.

BLOOD COUNTS

| Date. | Hem. | R. B. C. | W. B. C. | Index. | Poly. | Per cent. | Lymph. | Per cent. | L. mon. | Per cent. | Eosin. | Per cent. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1919: | | | | | | | | | | | | |
| 3/5 | 25 | 870,000 | 8,200 | 1.5 | 4,182 | 51 | 3608 | 44 | 410 | 5 | | |
| 3/9 | 25 | 720,000 | 5,000 | | | | | | | | | |
| 3/11 | 28 | 395,000 | 5,400 | | | | | | | | | |
| 3/13 | 10 | 239,000 | 5,000 | 2.5 | 2,900 | 58 | 1400 | 28 | 650 | 13 | 15 | 1 |
| 3/20 | 28 | 650,000 | 6,300 | | | | | | | | | |
| 3/22 | 15 | 730,000 | | | | | | | | | | |
| 3/24 | 15 | 820,000 | (five | .... | ..... | 66 | .... | 25 | .... | 9 | | |
| 4/3 | 20 | 488,000 | counts) | | | | | | | | | |
| 4/14 | 23 | 722,000 | | | | | | | | | | |
| 4/18 | 24 | 1,100,000 | 18,500 | .... | 16,650 | 90 | 1665 | 9 | 185 | 1 | | |
| 4/19 | 25 | 1,028,000 | 5,600 | .... | 4,200 | 75 | 1176 | 21 | 224 | 4 | | |
| 4/23 | 28 | 980,000 | | | | | | | | | | |
| 5/1 | 26 | 1,150,000 | | | | | | | | | | |
| 5/7 | 30 | 1,860,000 | | | | | | | | | | |
| 5/13 | 35 | 1,520,000 | | | | | | | | | | |
| 5/31 | 34 | 2,096,000 | | | | | | | | | | |
| 6/20 | .. | 1,056,000 | 8,400 | | | | | | | | | |
| 7/10 | .. | 1,470,000 | 7,600 | | | | | | | | | |
| 7/22 | .. | 1,831,000 | 4,800 | | | | | | | | | |
| 8/13 | .. | 2,400,000 | | | | | | | | | | |
| 9/7 | .. | 1,344,000 | 4,400 | 1.4 | 1,980 | 45 | 528 | 12 | 1804 | 41 | 88 | 2 |
| 9/17 | .. | 2,240,000 | 5,200 | | | | | | | | | |
| 11/10 | .. | 1,728,000 | | | | | | | | | | |
| 1920: | | | | | | | | | | | | |
| 1/15 | 42 | 1,880,000 | | | | | | | | | | |
| 3/3 | .. | 2,300,000 | 5,000 | .... | 2,550 | 51 | 2000 | 40 | .... | .. | 400 | 8 |
| 4/17 | 70 | 2,300,000 | 5,600 | .... | 4,368 | 78 | 448 | 8 | 672 | 12 | 112 | 2 |
| 5/6 | 55 | 2,225,000 | 5,500 | 1.25 | | | | | | | | |
| 6/4 | 55 | 2,176,000 | 4,800 | 1.267 | 2,784 | 58 | 864 | 18 | 960 | 20 | 96 | 2 |
| 12/9 | 80 | 3,882,000 | 8,200 | .... | 5,166 | 63 | 2624 | 32 | .... | .. | ... | 1 |

In several instances in which the differential count was made it is also recorded that there was poikilocytosis, anisocytosis, macrocytes and microcytes, basophilic degeneration, polychromatophilia, that the deeply stained macrocytes predominated, and that no neucleated red cells were found. Once the malarial parasite was sought and not found.

The sharp rise in the red cell count between the 14th and 18th of April, 1919 was the result of the transfusion on the 16th of April of 575 c.c. of blood. This was followed by a violent

reaction, rigors, pyrexia, tachycardia, headache, vomiting, and pain all over the body, and also a high polynuclear leukocytosis that disappeared by the third day.

The urine was normal throughout. One test for urobilin was negative. The phenolsulphonepthalein test was:

| | | |
|---|---|---|
| First hour | 110 c.c. | 40 per cent. |
| Second hour | 60 " | 18 " |
| Total | 170 " | 58 " |

There was a complete achylia gastrica.

On September 18th the patient complained of dizziness and marked weakness of the lower limbs. The appetite was poor. The bowels were regular and he was sleeping well. This relapse was temporary, for by October 4th the dizziness had disappeared, the appetite had improved, and he had been able to be out of bed for several hours every day. The legs were still weak. By the 11th he was still better, although there were still occasional spells of dizziness. This had disappeared by the 31st, but as a result of being up he had developed a slight edema of the feet. He had had a brief attack of diarrhea, which was ascribed to the arsenic, and ceased as soon as the arsenic was discontinued.

On March 13, 1920 he weighed 210 pounds, the skin was ruddy, actually a dusky pink, without a trace of cyanosis or yellowness. The mucous membranes were of a clear pink color. The legs, especially the left, were still numb. The vibratory sense was present in both legs, but impaired over the left tibia.

By April 17th he was able to work about the ward, but tired rather easily. The numbness in the legs was unchanged. His appetite was good and the bowels regular.

There was little distinct improvement after this. He spent nearly all day out of bed. He walked more, but still complained of weakness in his legs. A slight, almost doubtful, ataxia (finger-to-finger) in the hands was noted. The patellar reflex was delayed and weak.

In June the improvement was more distinct. He no longer complained of being tired, slept well, and spent all of the day out of doors.

There is nothing specially remarkable about this case of pernicious anemia. Lower counts have been recorded, particularly the one of Quincke of 143,000 red cells reported by Osler. If I can trust several of my residents, however, who made counts, unrecorded, unfortunately, during the early days of his stay in the hospital, the count actually dropped to below 100,000. In the absence of a record, of course, no definite statement can be made, but it is only another example of the importance of recording each observation as soon as it is made.

The case belongs apparently to the group of aplastic anemias associated with defective blood production. Neither is there anything in the least unusual about the remission. Cabot has shown that in more than half of the cases of pernicious anemia a remission occurs after the initial attack, and this remission may last for several years, so that our patient has broken no record up to the present time.

The nervous symptoms apparently were in their earliest stage. They did not increase after the fall of 1919, and it is possible that the increased activity of the patient is evidence that there has been improvement in the lower portion of the spinal cord. In this connection it may be mentioned that the patient has had enormous doses of arsenic over a long period of time, and that, therefore, a peripheral neuritis due to the arsenic as an explanation of these nervous disturbances can be wholly excluded, but at the present day no evidence is needed to prove that the anemias affect the cord and not any remedy that may be employed to cure them.

The ruddy color of the skin is more unusual. In my own experience I have not hitherto observed it to such a degree in pernicious anemia. In one case of chlorosis that I saw it was quite marked. It is not mentioned in most of the articles upon pernicious anemia. In the present instance there is a hyperemia disappearing momentarily after pressure. The patient is very much redder than the healthy skin ever is, and this color appeared long before the red blood-cells had reached 3,000,000. In the case of chlorosis that I saw the hemoglobin was below 50 per cent., and yet the skin was as red as it is in the present

patient. How to explain this I do not know except by stating that it is a cutaneous hyperemia, which is no explanation at all. In aërocyanosis, as it is called, we have a bluish or purplish color of the skin, and the blood return after pressure takes place slowly. In this instance it is an active hyperemia. Nevertheless, the blood count taken from blood drawn from the reddish skin indicates no excessive accumulation of red blood-cells in this area. In fact, all our blood counts have been so taken.

It was noted particularly by Draper, in a paper read in September, 1920, before the Pennsylvania State Medical Society, that many cases of pernicious anemia have disturbances of the endocrin system. Apparently there is no typical disturbance, but the disturbance in the ductless glands may be associated with disturbances of the blood-forming or blood-destroying organs. The present patient exhibits a rather unusual type. At the time of puberty the secondary sexual characteristics appear in the male and female, but differ fundamentally in the two sexes. In the male they consist essentially of the appearance of the pubic, axillary and facial hair, and the change in the voice; in the female in the appearance of the pubic and axillary hair, the development of the mammary gland, and the establishment of menstruation. Occasionally there are variations from the true type, usually that the secondary sexual characteristics develop in an abnormal way. Among these changes the commonest (at present known) is the so-called status thymicus, in which we find the pubic hair terminating in a transverse line as it does in the female, the axillary hair and beard very scanty. The opposite condition sometimes occurs in females with the pubic hair forming a triangle, pointing toward the umbilicus, with scanty development of the mammary gland or even remaining undeveloped as it is in children and males, and often the appearance of a moderate beard. In ancient sculpture figures are found frequently evidently of males with well-developed mammary glands of the feminine type. These were called hermaphrodites. It was doubted whether they were not purely imaginary, but this patient presents a precisely similar appear-

ance. You will observe that the breasts are well developed, hemispheric in shape, with well-developed large typical female mammæ. Upon palpation it can be determined that the breasts are largely fatty in nature and that surrounding the nipple there

Fig. 108.

is an area of denser tissue which resembles the normal glandular tissue. They have never, according to the patient, secreted any milk. Curiously enough, he is rather proud of them and took a great deal of interest and satisfaction in having them photographed.

No explanation of this condition is possible. We can state that presumably the gonads are so perverted that they have produced in one individual secondary characteristics of both sexes. It cannot be supposed that in this case the gonads are responsible for the pernicious anemia. It seems more reasonable to assume that the defect in one group of endocrin glands suggests defects in other groups, particularly those concerned with blood formation, and that the latter are directly responsible for the disease. Speculation is idle, but, on the other hand, frequently it leads to more careful observation, and if we can establish a more definite association between the endocrin glands and pernicious anemia it may lead to some improvement in the treatment.

At the present time in the aplastic type it can be assumed that the deficiency in the blood-forming glands is probably due to the bone-marrow. As I shall show, I have reached the conclusion that in these cases there is a double action, that is, that some hormone-like substance is required to stimulate the glands to form blood, that this hormone-like substance is probably present in the blood of healthy individuals. Where there is excessive activity of the blood-destroying organs we have learned that at least temporary improvement may occur when the chief organ of blood destruction, the spleen, is removed. We have here a parallel between myxedema and exophthalmic goiter. In one case there is glandular deficiency improved by substitution or hormone therapy, and the other functional glandular excess relieved by partial removal of the gland.

The fifth point I wish to discuss is the treatment that was employed. This was of four kinds. Unfortunately, it is not possible to discriminate between the effects of the different varieties of treatment employed, chiefly because these effects appeared so slowly that they may have been due to any one of them. On the basis that pernicious anemia may possibly be due to a focal infection we had the snags and teeth (at the roots of which abscesses had been demonstrated) removed. I have now in the wards another patient, also anemic, of a light brownish or lemon-yellow color, from the abscesses at the roots of whose teeth Streptococcus viridans was cultured. I have observed no less

than 3 cases of profound anemia from the blood of whom Streptococcus viridans was obtained. Libman has called attention to the grayish color which he believes almost pathognomonic in patients suffering from streptococcic endocarditis. There seems to be no doubt that at least a moderate degree of anemia may be caused by infection from the hemolytic micro-organisms. Unfortunately, cultures were not made from our patient's teeth, and we do not know whether there is any warrant for supposing the focal infection was responsible for the condition. In the wards of this hospital considerably more than 90 per cent. of the patients admitted have oral sepsis, and it is therefore difficult to assume that it is a definite cause in a condition comparatively as rare as this.

Transfusion was also employed. In the case of aplastic anemia this appears to be our only available remedy, as splenectomy rather hastens than retards the fatal termination. I spoke before of a possible existence in the blood of a hormone. I wish now to cite a case that I think supports this belief.

This patient was first seen when fifty years of age. He had then felt weak for nearly a year. He had all the appearances of advanced pernicious anemia—hemoglobin 20 per cent., red blood-cells 1,580,000, white blood-cells 3000. There was a complete achylia. The blood coagulated rather slowly. On medical treatment, chiefly arsenic, he made some improvement. The blood reached 3,330,000, the white blood-cells 3800. The differential count showed a preponderance of polymorphonuclear forms, an unusual feature. There was no excess of bile in the feces and no occult blood. In two months he had gained 17 pounds in weight and, aside from some numbness in the legs, he felt stronger. The blood count had risen to 4,460,000, with 81 per cent. hemoglobin. Four months later he had relapsed badly. The blood count was now 40 per cent., red blood-cells 2,510,000, and the white cells 4700, a rather persistant leukopenia. As he failed to improve and the red blood-cells decreased below 2,000,000, with only 28 per cent. hemoglobin, it was decided to perform a transfusion, this in spite of the fact that he was still gaining weight slightly. The first transfusion was

performed on April 20th. The blood counts immediately afterward were:

4/22: Hb. 20 per cent., red blood-cells 1,560,000, white blood-cells 3850. Lymphocytes 38 per cent.
4/24: Hb. 20 per cent., red blood-cells 1,310,000, white blood-cells 3150.
4/26: Hb. 20 per cent., red blood-cells 1,630,000, white blood-cells 3920.

The second transfusion was performed on May 5th. and the blood counts immediately before and afterward are as follows:

| | | | | |
|---|---|---|---|---|
| 5/2 : | Red | blood-cells, | | 710,000 |
| 5/4 : | " | " | " | 1,160,000 |
| 5/6 : | " | " | " | 2,020,000 |
| 5/10: | " | " | " | 2,036,000 |
| 5/12: | " | " | " | 1,750,000 |

The third transfusion was done on May 16th, with the following results:

| | | | | |
|---|---|---|---|---|
| 5/16: | (Before) | red | blood-cells, | 1,370,000 |
| 5/17: | (After) | " | " | " 1,390,000 |
| 5/18: | | " | " | " 2,060,000 |
| 5/21: | | " | " | " 2,690,000 |
| 5/23: | | " | " | " 2,000,000 |

What the immediate effect of the first transfusion was, unfortunately, we cannot tell. The blood count in my office on April 19th was hemoglobin 28 per cent., red blood-cells 1,290,000, white blood cells 5600. There was a slight increase two days after the transfusion, which persisted until six days after the transfusion, and then steadily declined. After the second transfusion there was a marked increase in two days. This continued for six days and then there was a rapid decline. After the third transfusion there was no increase the first day, marked increase on the second day, which was still more pronounced on the fifth day. From this time there was persistent improvement until the blood, without further treatment, had reached practically a normal count.

The interesting feature in these three observations is that the maximum effect of the transfusion did not occur immediately. It was not the addition of corpuscles to the blood that helped

the patient, but something in the transfused blood that stimulated his own blood-forming glands to greater activity, and finally produced a degree of stimulation that caused them to continue acting over a long period of months during which time he felt, with the exception of some numbness of his legs, entirely well.

The subsequent history of this case is not so happy. During my absence at the war he was treated by another physician, who had a splenectomy performed, after which his blood rapidly deteriorated. He developed a complete paraplegia, and in the course of a few weeks died without experiencing any benefit whatever. I merely cite this case, first, as a concrete example of the somewhat tardy improvement that follows transfusion, the strongest effects of which are not felt, as a rule, until four or five days afterward; second, of the benefit of transfusion as compared with the injury of splenectomy.

In the present case of aplastic anemia there were two other forms of treatment employed. The patient was given huge amounts of arsenic. This was given in the form of cacodylate of sodium, from $\frac{1}{2}$ to 1 grain hypodermically twice a day, or in the form of Fowler's solution, 8 drops three times a day. The longest period of administration was nine months, during which 8 to 10 drops of Fowler's solution were given three times a day uninterruptedly, but the Fowler's solution was given for more than two months on one occasion and for more than a month several times. At no time, with the exception of a transient diarrhea, was there any evidence that the arsenic did harm. He complained of no indigestion, showed no pigmentation or evidence of polyneuritis. There was no increase, as I have already noted, of the signs in the legs. I have not attempted to calculate the total amount of arsenic that he received in the course of a little more than a year, but it was very considerable. Possibly these large persistent doses of arsenic may be in part responsible for the ruddy color. He has also taken dilute hydrochloric acid in very large doses over long periods of time. The usual dose was 1 fluidram of the dilute or 10 per cent. hydrochloric acid given well diluted three times a day either before or after meals. It also can be said to have manifested no injurious effect. Although

he had achylia, his weight increased fairly considerably during its administration. Unfortunately, he was not weighed on admission. At that time he was a poorly nourished man. Now, with a weight of 210 pounds, he is distinctly obese. How long the present remission will last we cannot, of course, tell, but as he is content to remain in the hospital, earns his board and lodging by working cheerfully and industriously in the wards, and feels quite confident that he could not earn his living outside, it is possible that we may be able to follow the course over a period of years.

## CLINIC OF DR. GEORGE WILLIAM NORRIS

PENNSYLVANIA HOSPITAL

### TOPHACEOUS GOUT

**Chief Complaint.**—The patient before you, a widow, sixty-three years of age, Anglo-Saxon in type, the third generation of her family to be born in this country, comes to us complaining of pain in the arms and legs and painful swelling of her fingers, elbows, and knees.

**Family History.**—Her mother suffered from "rheumatism" and died of pneumonia. Her maternal grandfather had "rheumatism" of such severity that he had to periodically use crutches. He had, however, intermissions between attacks when he was quite well and had no disability whatever. The other data are unimportant.

**Past History.** The patient has never been robust. In addition to the diseases of childhood she has had "malaria," the last attack six years ago, and "influenza" one year ago.

She has suffered from headaches all her life, especially during menstruation, and has been much troubled with hot, burning and stinging eyeballs, with lacrimation. Most of her teeth were extracted three years ago.

All her life she has had trouble with "cold on the chest," often with expectoration, sometimes blood-streaked. Recently she has had night-sweats. Her best weight, twenty years ago, was 135 pounds. She now weighs 85 pounds. She had one child which died in infancy. The menopause occurred at forty-five years of age.

**Present Illness.**—About three years ago the patient began to have sharp pains in her arms, in the back, and in the nape of the neck. These symptoms have gradually increased, with

periods of intermission and exacerbation, the latter being associated with damp weather.

Two years ago she began to notice that her fingers were swollen, and that small nodules were developing in her hands, elbows, and knees. These nodules were painless unless subjected to trauma. She has been in moderate circumstances financially, has never been a heavy eater, or indulged in alcoholic beverages to any extent. She now complains of sharp pains in her arms and legs, stiffness of the back of the neck, and cramp-

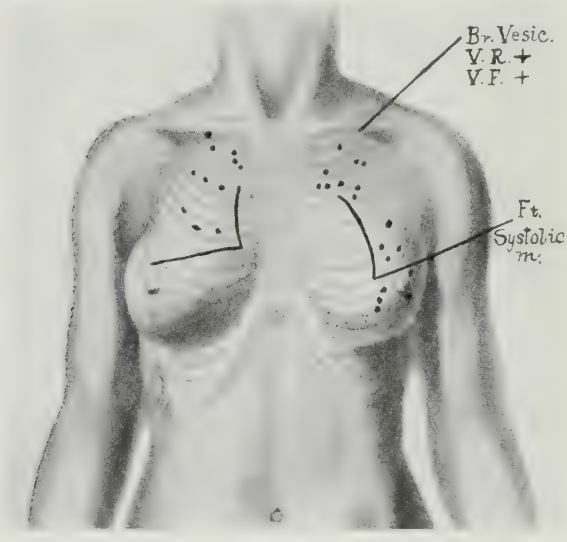


Fig. 109.

like sensations in the toes, which are, however, not tender to pressure.

**Physical Examination.**—The patient is a pale, markedly emaciated, white female, age sixty-three years, sitting up in bed, apparently not in any pain, not jaundiced, dyspneic, cyanotic, or edematous. *Skin:* Loose and wrinkled, dry, and of poor tone. *Head:* No evidence of injury. *Eyes:* Conjunctivæ slightly injected. *Nose:* Normal. *Ears:* Auricle rather scaly, no gouty nodules. *Accessory sinuses:* Normal to routine examination. *Mouth:* One decayed root above, none below, tongue

not coated, protrudes in midline. Slight amount of tonsillar tissue present. Pharynx slightly injected. Hard, irregular, pea-sized nodules on each side of mental tuberosity; firm, and not very freely movable. *Neck:* Long, thin, muscles prominent, skin loose and wrinkled. No rigidity. Anterior cervical glands palpable. Suprasternal notch and supraclavicular fossæ deep. Veins visible and pulsating. Moderate carotid pulsation. *Chest:* Very much emaciated, skin loose and flabby, flat type. Ribs prominent, interspaces sunken, costochondral articulations and

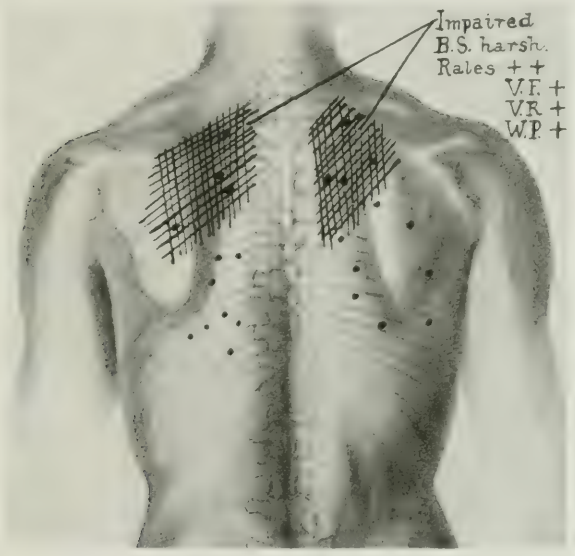


Fig. 110.

angle of Louis prominent. Left side of chest larger. Clavicles stand out markedly. Excursion fair. Expansion poor. Apex-beat diffuse; palpable 13 cm. from M. C. L. in fifth left intercostal space. Note hyperresonant, high pitched on left side and in axilla, hyperresonant in right axilla. Many râles all over chest; fine crackling variety (Figs. 109, 110). *Heart:* Left border 14 cm. to left of midsternal line in fifth intercostal space. Right border 2 cm. to right of midsternal line, level of third intercostal space. $P^2+$ and reduplicated. Thrill felt at apex systolic (?)

in time. Very faint systolic murmur at apex. Apical sounds loud and of good quality, rhythm regular. *Abdomen:* Lower abdomen full and tympanitic. Venous distention present. Linear striæ present. Exostoses (?) on iliac crests. Abdomen rather tense, not much distended, no tenderness, no masses felt. Spleen and liver not felt.

*Spine.*—Some lateral curvature present, prominence of some of the spinous processes. Spine rigid from tenth to about first dorsal vertebra.

*Arms.*—Emaciated, calcareous deposits around each elbow-joint and in ligaments; marked thickening of fingers and deformities of knuckles; marked calcareous deposits about joints and tenderness of fingers; left wrist slightly painful. Moderate arteriosclerosis.

*Legs.*—Slight limitation of motion in left hip-joint, motion is painful. Both knees have marked calcareous deposits about articular surfaces of joints. Marked crepitation elicited. Motion limited slightly. Ankles and toes not much affected. No edema of legs or scars present.

*Reflexes.*—Knee-jerks, biceps and triceps present and normal. Babinski, ankle and patella clonus, and Achilles negative.

Dr. Norris: With such a history as has just been read, what ailment is suggested?

A Student: Rheumatoid arthritis.

Dr. Norris: Can you think of any other condition?

A Student: Gout.

Dr. Norris: Notice that the disease dates back over several years, with exacerbations, often influenced by barometric changes, and that the small joints of the hands are chiefly involved.

Inspection reveals a large number of hard, irregularly rounded yellowish nodules, quite symmetrically disposed. They are not at present particularly painful or tender. They are subcutaneous, more or less freely movable, and attached to fibrocartilaginous structures, such as tendon sheaths and aponeuroses.

On the palmar surface of both hands you will note along the course of the flexor tendons of the first and second fingers such

Fig. 111.—Palmar surface of the hands showing tophi.

Fig. 112.—Tophi on the elbow and chin. The left side of the body showed symmetric involvement.

masses having the size of very large peas. Note also the thickening and deformities of the phalanges. There are, however, no

destructive changes in the joints, and movement is not very greatly restricted. The deposits are outside rather than inside the joints, and they occur in some instances along the tendon sheaths, far distant from the articulations (Fig. 111).

Both elbows show marked deformities overlying the olecrani, as do also the prepatellar regions. In the latter areas you will

Fig. 113.—Tophaceous deposits in the prepatellar regions. Note also operative scar and the dried chalky discharge therefrom. Deformity of fingers is shown from the dorsal surface.

notice large bony plaques, having a more or less diamond shape, about 5 cm. in length and 0.5 cm. in thickness. The surface is studded with irregularly rounded elevations about 0.5 cm. in height. The skin overlying these excrescences on the elbow is dark red and seems acutely inflamed (Figs. 112, 113).

For purposes of comparison and contrast I will pass around a photograph of a characteristic and typical case of rheumatoid

arthritis, with involvement of the elbows, knees, ankles, wrists, and hands (Fig. 114). You will note at once the complete dissimilarity between the photograph and the case before us.

Fig. 114.—Rheumatoid arthritis. Involvement of the ankles, knees, elbow, wrists, and hands. Note the characteristic shape and deformity of the fingers and the wasted muscles of the forearm, hand, and calf.

But to return to our patient. On either side of the jaw-bone about 4 cm. back from the symphysis two rough irregular tesselated masses about the size of a pea can be seen.

Scattered over other different portions of the body similar deposits can be noted. Thus, along the edge of the tibiæ and the

ulnæ roughened miliary elevations occur; also on the trochanters; and when the thighs are flexed, crepitation can be felt.

Upon the luminescent screen you will see a number of *x*-ray negatives which Dr. Bowen has furnished us.

Fig. 115.—Radiogram of the hand showing tophi. Note involvement of the wrist as well as of the fingers. Compare with Fig. 111. (Courtesy of Dr. D. R. Bowen.)

You will note that these deposits have a great density, much like that of bone itself (Figs. 115–117).

Now notice that in some respects this case—if it be one of

tophaceous gout—is atypic. The ears have escaped entirely, as have also the feet. Furthermore, the patient gives no history of acute attacks involving the great toe. We must remember, however, that gout is protean in its manifestations. Some cases have marked, recurrent, acute seizures, with only moderate deformities; some have marked deformities with only moderate pain; and

Fig. 116.—Radiogram of the elbow. Compare with Fig. 112. Note deposits along the periosteum of the ulna. (Courtesy of Dr. D. R. Bowen.)

some have scarcely any joint involvement, but suffer from migraine, "sick headaches," "biliousness," neuralgia, if not actually neuritis, and many other bizarre manifestations.

Over the left patella you will notice an incised wound, surrounded by an area of erythema, which has not yet healed. One week ago for diagnostic purposes, with due antiseptic precau-

tions, Dr. Marsh removed one of these calcareous masses. The wound did not heal by first intention, but soon broke down and for several days discharged a considerable amount of white cretaceous material having the consistency of cream, with which the surrounding tissues were apparently saturated. The wound shows but little active inflammatory reaction and is slowly healing by granulation.

Fig. 117.—Radiogram of knee. Compare with Fig. 113.

Now let me read you Dr. Phillips' report on the excised specimen:

"The specimen consists of a small, irregular, soft mass of tissue in which there are circumscribed chalky white areas of a rather soft mortar-like material. Other small softened mucoid foci are also present."

**Microscopic Examination.**—"Sections through the tissue submitted reveal a dense fibrous tissue framework which has undergone hyaline degeneration in many places and contains

circumscribed empty spaces whose borders have undergone calcification. The soft material has escaped from the cavities. No sodium biurate crystals characteristic of gouty tophi are seen. Upon the addition of sulphuric acid colorless needle- and plate-like crystals are formed along the calcareous borders, indicating the formation of calcium sulphate."

**Diagnosis.**—"Dense fibrous tissue which has undergone calcification and necrosis—probably an old gouty tophus."

**Routine Laboratory Findings.**—*Urine:* Acid, 1011–22; albumin, trace; glucose, 0. No casts.

*Blood:* Hb., 60 per cent.; erythrocytes, 3,512,000; leukocytes, 5800.

*Blood Wassermann:* Negative.

The patient has been afebrile, with a blood-pressure of 140–80.

In the case before you the diagnosis of tophaceous gout is, I think, justified and easy, but often, especially in the atypic cases, many mistakes are made. Some practitioners too readily attribute symptoms for which no apparent cause exists, and which may be due to undiscovered focal infections—to gout. It is very easy to fall into this habit, particularly when a patient comes from a family with gouty tendencies. Gout often, if not usually, comes by inheritance. Of course, some one must have "started it." Also one sees individuals who by gross overeating and drinking, together with insufficient exercise, have brought it on themselves. But many people whose habits of life conform to this standard never develop gout.

Dr. Norris: What do you understand by the term "gout"?

A Student: A constitutional disturbance of purin metabolism.

Dr. Norris: Yes. A disturbance by virtue of which uric acid fails to be promptly eliminated from the blood so that sodium urate becomes deposited, especially about the fibro-cartilaginous structures where the circulatory currents are slow. Under normal conditions the blood contains about 1.7 mg. of uric acid per 100 c.c. In the present case blood analysis showed 2.5 mg. per 100 c.c.

It would seem, however, that a simple increase of uric acid alone is not solely responsible for gout, because an increase has been shown to occur in different conditions, such as leukemia, pneumonia, and nephritis, without gouty symptoms.

As a rule one finds the urinary output of uric acid diminished before an attack of gout. Between attacks the excretion may be normal or but slightly decreased, but in some tophaceous cases it may, according to Futcher, be entirely absent. Coincident with the beginning of an attack the output is usually much increased.

As to the cause for this accumulation of uric acid in the system there is still much lack of knowledge, but opinion seems to be veering around to the view that it is due to a change in renal permeability which results in an elevation of the threshold of excretion. The uric acid in the blood is derived from a two-fold source: first, that due to endogenous metabolism; second, the exogenous moiety, that resulting from the eating of purin-containing food. The endogenous purins on a purin-free diet are quite constant for a given individual. They represent wear and tear of the body and are derived from the nuclei of body cells which have undergone destruction. The exogenous purins, of course, vary with the quantity of purin-containing food ingested, this coming from two sources, the nuclei of cells and free purins, such as hypoxanthin, existing in muscular tissues. What varieties of food furnish the largest amount of uric acid?

A STUDENT: Red meats.

DR. NORRIS: Has any one else any suggestions?

A STUDENT: Sweetbread.

DR. NORRIS: Yes. Generally speaking, the glandular organs of the body—thymus, pancreas, liver, kidneys—yield the largest amount and are, therefore, the most undesirable from a gouty man's standpoint.

On the blackboard you will find a list of the more important purin-containing foods. One kilogram of the flesh of cod contains approximately 0.5 gm. of purins. This appears in the table as 1 unit.

PURIN CONTENT OF ANIMAL FOODS. (I. W. HALL.)

| | | | |
|---|---|---|---|
| 1 unit: | Tripe. | 2½ units: | Turkey. |
| | Cod. | | Chicken. |
| | | | Beef (sirloin). |
| 1½ units: | Plaice. | | |
| | | 4 units: | Beefsteak. |
| 2 units: | Mutton. | | |
| | Rabbit. | | |
| | Halibut. | | |
| | Pork. | 6 units: | Liver. |
| | Beef (ribs). | | |
| | Ham. | | |
| | Veal. | 20 units: | Sweetbreads (thymus). |
| | Salmon. | | |

PURIN CONTENT OF VEGETABLE FOODS (CONTAINING MORE THAN A TRACE)

| | |
|---|---|
| Two-fifths unit: | Asparagus. |
| Four-fifths unit: | Pea-meal. |
| One unit: | Oatmeal. |
| Six-fifths unit: | Beans. |

Some physicians forbid red meat, but allow white meat, although the rationale of this is open to question. Chemically the difference is not great. If we tell our patients that they may eat white meat they often do so in excess, and do themselves more harm than they would by a small quantity of red meat.

Quantity is quite as important as quality. The gouty patient, if he would minimize his attacks, must live simply. He must eat no more than enough to supply his daily metabolic requirements. Rich, highly seasoned foods, malt liquors, wines, especially of the port type, are to be absolutely forbidden. The diet should be mainly of the cereal, milk, and vegetable type. But again certain vegetables and fruits, notably those which contain much oxalic acid, are often harmful, although there is much individual variation about this.

But gout is not only a question of diet. Our patients must have regular exercise of as an active variety as the patient's general condition will permit. Freedom from worry, anger, overfatigue, or shock is necessary, for such conditions not infrequently precipitate an attack. It is not sufficiently appreciated that prolonged or extreme nervous strain—anything which tends to

lower general nerve tone—favors the occurrence of gout. Many gouty individuals, especially those who are of a high-strung temperament and an asthenic constitutional habitus, do themselves more harm than good by the extreme use of severe physical exercise or too frequently repeated and prolonged Turkish baths.

Furthermore, we must not forget that there is such a thing as poor man's gout which is due to poor food, bad hygiene, and an excessive consumption of malt liquor.

Now let us consider another phase of the case. You will remember that our patient states that she has had poor health all her life, with attacks of bronchitis, "malaria," and "influenza," and that she has lately lost much weight. The physical signs as found on examination of the chest are graphically depicted on these charts (Figs. 109, 110). They show evidences of pulmonary infiltration, especially at the apices, with numerous diffusely scattered râles, together with chest deformity and poor expansion. Based upon such physical signs one would be justified in assuming a long-standing chronic pulmonary tuberculosis with secondary fibroid changes.

Fluoroscopic examination fully confirms this hypothesis. The apices are somewhat dense. The hilus shadows are accentuated and plates show peribronchial thickening with numerous calcified lymph-nodes, and marked calcification of the tracheal rings.

Now, what relation, if any, exists between gout and tuberculosis?

There is much clinical evidence which indicates that gouty people do not often develop tuberculosis; and, *per contra*, that no matter how much nitrogenous food a tuberculous person may consume, he will not become gouty.

Is it not possible that our patient acquired tuberculosis early in life, but that her gouty diathesis prevented the disease from becoming acute, and brought about these fibroid processes which are generally considered to indicate resistance to infection, and which often result in a functional cure?

The râles which were so numerous in her chest at the time of admission, and which might have suggested the possibility of a

general miliary tuberculosis, have largely disappeared. They appear to have been due to an acute bronchial infection, a condition to which gouty people are frequently subject.

What effect does long-standing gout have upon the system? What tissues are chiefly affected.

A STUDENT: Nephritis.

DR. NORRIS: I see that you remember your pathology—"gouty kidney." Yes. You will remember that the kidney is small, shrunken, shriveled, dark red and granular in appearance, with an adherent capsule. Similar lesions are produced by chronic lead-poisoning, cachexia, focal infections, etc. In the present case you remember we found a trace of albumin in the urine, but no casts and no hyposthenuria. The phthalein elimination was 30 per cent. in the first and 20 per cent. in the second hour.

We must try to explain our patient's 50-pound loss of weight. We have to explain it: first, fibroid tuberculosis; second, arteriosclerosis with some renal involvement; third, loss of teeth.

Which of these factors plays the predominant rôle?

This is a difficult question to answer. Arteriosclerotics, especially those in whom the renal lesion is considerable, often show marked emaciation in the late stages.

The treatment of gout is essentially dietetic and hygienic, but during the acute seizures other measures may be employed with benefit.

Local applications, especially heat, are beneficial.

What drugs are most useful?

A STUDENT: Blue mass and a saline purge.

DR. NORRIS: Yes, this is often a useful preliminary. Can you think of any others?

A STUDENT: Salicylates.

DR. NORRIS: Sometimes they may do good, but generally one gets better results from colchicum, given in 20- to 30-minim doses until purgation occurs. A man whom I once knew, who had had his first attack of gout in the great toe at the age of thirteen, and had been a frequent sufferer from gout during the remaining seventy years of his life, who had consulted many

doctors and had tried all sorts of quackeries, had lost all faith in remedies except colchicum, which he said "always cuts short my attacks if I take enough of it, and until it acts there's nothing to do but grin, if you can, and bear it."

Similar testimony is given by many sufferers from this disease. So far as known, colchicum has no definite effect upon uric acid excretion either in health or in gout, but it seems definitely established that it helps to relieve pain and shorten the attack of an acute seizure, and further, that this is not merely the result of the purgation which its irritation of the gastro-intestinal mucosa produces.

## CLINIC OF DR. ELMER H. FUNK

JEFFERSON HOSPITAL

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# THE DIAPHRAGM: ANATOMIC AND PHYSIOLOGIC CONSIDERATIONS; METHODS OF EXAMINATION; CONDITIONS ASSOCIATED WITH ALTERED POSITION OF THE DIAPHRAGM; DIAPHRAGMITIS

I WISH to call your attention today to a structure often neglected in the study of respiratory disease, namely, the diaphragm. It is difficult to explain why an organ of its importance should be so frequently left out of consideration or, at most, only casually investigated in the usual physical examination. It may be because lesions of it are, for the most part, secondary to other lesions which claim the principal attention. And yet a complete conception of the many respiratory diseases and disorders is not possible without an estimate of its anatomic and functional integrity. It is the "great muscle of respiration," and the more one studies it, the more it assumes an importance approaching that of the "great muscle of circulation"—the heart. The time was when the latter was considered of secondary importance to a consideration of valve defects. Now the consideration of the cardiac muscle has assumed the all-important position and the actual valve defects a secondary rôle. At the present time I fear the relation of the diaphragm to respiratory disease is in the position of the heart muscle prior to the present time. I want to voice here the prophecy that there will be an increasing attention paid to this structure in the years to come. My friend, Dr. Landis, of this city, and Dr. Hoover, of Cleveland, are among those who have called attention in recent years to the need for careful study of the diaphragm.

Perhaps it may seem rather elementary to review briefly certain anatomic and physiologic considerations with regard to the diaphragm, and yet this basic knowledge is necessary if we are to comprehend (1) the methods of examination, (2) the rôle it plays in disease, and (3) the lesions which result from its proximity to other organs.

## ANATOMIC AND PHYSIOLOGIC CONSIDERATONS

The diaphragm originates in embryonal life in the region of the neck and maintains its cervical relations through its innervation by the phrenic nerves which spring from the third to the fifth cervical nerve on each side. If you will study the two anatomic charts which I am showing you will note that the diaphragm is quite dome-like in shape, that it really consists of two muscles, each of which arises from the ensiform anteriorly, the cartilages and tips of the last six or seven ribs laterally, and from the sides of the lumbar vertebra posteriorly, and is inserted into the firm aponeurosis or central tendinous sheet. Laterally the diaphragm muscles project into the thoracic cavity higher than the central tendon, reaching in the average adult the level of the fifth rib on the right side and the fifth interspace on the left side upon moderate relaxation (expiration). The central tendon is less mobile because of its attachment to the pericardium and the heart. The diaphragm is in close association with the lining membranes of the four large serous cavities: the two pleuræ, the pericardium, and the peritoneum. Between the serous membranes and the diaphragm, both on the thoracic and the abdominal sides, are exceedingly rich plexuses of capillaries which freely connect with vessels which traverse the muscles. There is, however, only slight communication between the plexuses of the right and left diaphragm. Morris states that the lymphatic vessels empty into three groups of small nodes on the convex surface. The *anterior* group lies in front of the central tendon. Two or three nodes in the center of this group receive afferents from the liver and none from the diaphragm, but the rest receive vessels from the anterior surface of the diaphragm and the efferents of all pass to the lower set of anterior

mediastinal nodes. The *middle* group consists of from three to six nodes, which lie, on the left side, near the point where the phrenic nerve enters the diaphragm; on the right side, near the vena cava. The *posterior* group of four or five nodes is placed between the pillars of the diaphragm. The vessels from the lateral and posterior groups pass to the posterior mediastinal nodes, and also to the upper celiac nodes, which likewise receive the drainage from the posterior part of the abdominal surface of the diaphragm.

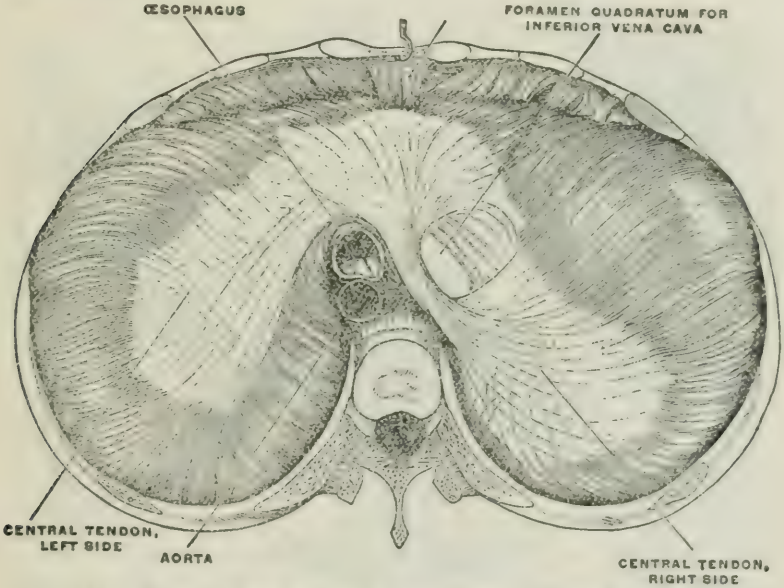


Fig. 118.—The diaphragm viewed from above. (Poirier and Charpy.)

When the diaphragm muscles contract the central tendon is drawn downward, with the resulting increase in the vertical diameter of the thorax. This movement occurs simultaneously with the action of other muscles, principally the external intercostals, which elevate the ribs, causing an enlargement in the anteroposterior and lateral diameters. The descent of the diaphragm is not directly downward, but downward and forward. It is, in reality, compounded of two movements, the spinal segment of the muscles causing a vertical elongation of the

thorax, while the sternocostal part pushes the abdominal viscera downward and forward. Since the diaphragm is attached to the lower ribs, there is a tendency during its contraction for these to be drawn inward and upward, but this diaphragm action is opposed by the scaleni and external intercostals which elevate and rotate them outward. In other words, if you observe the subcostal angle and its costal margins you will notice normally a widening of this angle on inspiration due to the flaring out of the costal margins.

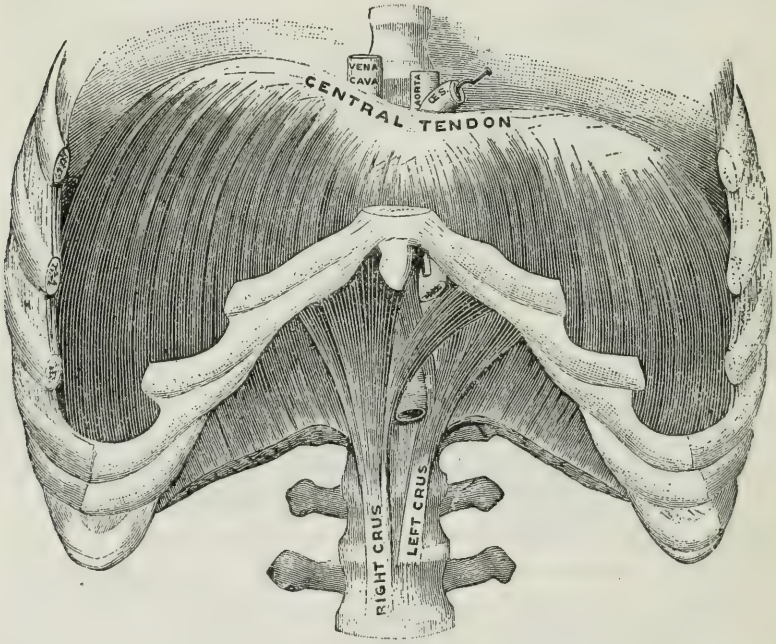


Fig. 119.—The diaphragm viewed from in front. (Testut.)

The nerve mechanism of respiration is extremely complex, but for the purpose of our clinical discussion this morning it may be briefly stated as follows: There is a bilateral center located in the spinal bulb which presides over the intricate co-ordinated movement of each half of the chest. This center is brought into relation with the respiratory muscles principally by the phrenic nerves to the diaphragm and the intercostal nerves to the muscles which elevate the ribs. The respiratory

center is also affected by impulses from a large number of afferent nerves, of which the most important are the pulmonary and laryngeal fibers of the vagus. Animal experimentation has shown that section of the spinal cord above the origin of the phrenic nerves causes paralysis of respiration and consequent death. Section of the spinal cord below the lesion of the phrenic nerves leaves the diaphragm working, although the other respiratory muscles are paralyzed. Since there are two phrenic nerves supplying corresponding halves of the diaphragm, section of one may be associated with unilateral paralysis. Irritation of the phrenic nerve produces spasm of the corresponding diaphragm muscle. Some physiologists hold that the phrenic nuclei in the cord are connected across the middle line, so that even in the presence of a lesion destroying one-half of the cord above this point, impulses are still able to reach both phrenic nerves.

A knowledge of the regulation of respiration is not complete unless one understands the relationship of that great afferent nerve, the vagus, to the respiratory movements. Section of both vagi results in a slowing and deepening of respiration. As a result of the section other afferent nerves from upper paths appear to take up the regulation of the respiratory movements. If for any reason these also should be interrupted, the respiratory center passes into a condition of alternating spasm and exhaustion. We shall have occasion a little later on in this clinic to call attention to disorders of the diaphragm resulting from disturbances of its innervation, but before we do let us turn for a few minutes to a consideration of the clinical methods of examination.

### THE CLINICAL METHODS FOR EXAMINATION OF THE DIAPHRAGM

**Inspection.**—*The Diaphragm Sign Of Litten.*—When the diaphragm is moderately relaxed, as occurs in expiration, its lower lateral portions are in close proximity to the chest wall. Litten in 1892 called attention to the fact that it was possible to observe externally the phenomena of the separation of the diaphragm from the chest wall during inspiration. The patient

is placed upon his back with chest bared and with the light at the foot or side of the bed. If the diaphragm movement is unimpeded there will be noticed on full inspiration that a horizontal shadow moves from the sixth interspace to the eighth or ninth interspace with inspiration. During expiration the shadow recedes again to where it started. It may be seen in some cases in the epigastrium. It is present in practically all normal individuals and is most clearly made out in young, lean, muscular individuals with good expansion. It is occasionally absent in health in those individuals who are short and stout with an abundance of subcutaneous fat, and are unable to make deep inspiratory and expiratory movements. The diaphragm shadow appears in the sixth interspace with the inspiratory separation of the diaphragm from the chest wall and disappears as the separation is filled by the descending wedge of lung tissue. As it disappears from the sixth it appears at the seventh, and so on, until it appears and disappears as low as the eighth or ninth interspace. The shadow is absent in all conditions which interfere with "the peeling off" movement—*e. g.*, in solidification of the lower lobe, in marked emphysema, in pleural adhesions and effusions. It is present in hepatic and splenic enlargements, in subphrenic abscess, and thus serves to help in the differential diagnosis of lesions above and below the diaphragm.

**Palpation.**—*The Movement of the Costal Margins of the Subcostal Angle.*—In the normal individual there is a moderate widening of the subcostal angle due to divergence of the costal margins upon inspiration. You will recall the balancing mechanism about which I spoke to you a few minutes ago in discussing the anatomic and physiologic factors of respiration. The tendency of the diaphragm to pull inward along its anterior and lateral insertions is more than overcome by the outward flaring of the margins of the subcostal angle by the action of the scalene and intercostal muscles. When, however, the diaphragm is placed at a greater mechanical advantage, as occurs when it is lowered in position, it secures a power which equalizes or overcomes the scalene and intercostal muscles and a fixation or actual narrowing of the subcostal angle occurs upon inspiration.

The reverse is likewise true, namely, when the diaphragm is placed at a mechanical disadvantage such as occurs in certain high positions—*e. g.*, eventration, subphrenic abscess—or when

Fig. 120.—Method of palpating the costal margins. The chest and lower abdomen are bared; the thumbs are placed along the costal margins of the subcostal angle and their movement noted with inspiration and expiration. Normally an inspiratory widening which is equal on both sides occurs.

the muscle is paralyzed as a result of a lesion—*e. g.*, of the phrenic nerve—the intercostal muscles acting unopposed produce a greater widening of the subcostal angle than normal resulting in exaggerated flaring of the costal margins. The

altered movements of the costal margin may be bilateral or unilateral, depending upon the bilateral or unilateral alteration in the conformation of a diaphragm dome. In observing the movements of the margins of the subcostal angle palpation is of greater aid than inspection. You will note the position (Fig. 120) in which the patient is placed—the baring of the lower chest and upper abdomen—the position of the hands with the thumbs pointing toward the ensiform cartilage and resting upon the costal borders of the angle. The patient is asked to breathe a little deeper than normal and the movements of the thumbs are visible and felt. I want to urge upon you to practice the method in every case and after a while you will obtain a skill in detecting minor variations which it is not possible at first to determine. Now watch my thumbs closely as I endeavor to elicit the movements in this patient. You will observe that there is a widening of the subcostal angle on inspiration, but that the left costal margin moves less distinctly than the right. The patient has a greatly enlarged heart, the diaphragm, especially on the left side, is pushed down—is lower than normal—and by reason of its lower position is at a greater mechanical advantage than its fellow of the opposite side, and in contracting is able to pull more forcibly, thus opposing more effectually the "flaring or widening" action of the scalene and intercostals. Our conception of the low position of the left half of the diaphragm is in this case verified by the *x*-ray study.

Dr. Hoover has recently written upon this subject again, and I would recommend to you the reading of his article in the Oxford System of Medicine by Christian and Mackenzie. To use his words, "Emphysema of both lungs will cause flattening of the entire phrenic dome. Unilateral pleurisy with effusion and pneumothorax will diminish convexity of one-half of the diaphragm. Pericarditis with effusion will flatten the entire subcardial diaphragm and leave the lateral and posterior portions unmodified. Enlargement of the left ventricle will depress the subcardial portion of the diaphragm to the left of the median line much more than to the right of the median line. Dilatation of the right ventricle and right auricle will

depress the subcardial diaphragm to the right of the median line much more than to the left of the median line. Convexity of the entire diaphragm may be increased by ascites or tympanites; the right half of the diaphragm may have its convexity increased by enlargement of the liver; while the left half may have its convexity increased by tumors of the spleen or stomach. Subphrenic abscess may also increase the convexity of either side. In obsolete pleurisy there may be a shortening of the longitudinal diameter of the thorax and an increase in the concavity of the under surface of the diaphragm. But in these cases there are always synechia between the diaphragm and the chest wall, and consequently the diaphragm is given a new point of insertion; instead of being at the end of the ribs, it will be at the inner surface of the chest wall. So, although the under surface of the diaphragm may have its concavity increased, there is lessened convexity of the upper surface of the effective portion of the diaphragm."

The movement of the costal margins is not diagnostic of diseases above or below the diaphragm except in so far as it gives us evidence as to the conformity of the vault of the diaphragm which is so often altered in these diseases. I remember very well sitting at the bedside of a patient with the late Dr. Francis T. Stewart when I was his house surgeon and have him explain to me the value of an observation of the movements of the lower costal margins in the estimate of the anatomic and functional integrity of the diaphragm in suspected disease in its vicinity, a lesson which in after years was impressed upon me by the writings of Hoover.

**Percussion.**—*To Determine the Diaphragm Movement.*—The position of the diaphragm, and more particularly the movement of the diaphragm, can be demonstrated by percussion of the lower pulmonary borders. And since from our previous discussion of the anatomy and physiology we learned that the vertical movement of the diaphragm was greater posteriorly than anteriorly, our percussion examination is directed more particularly to this area. The wider range of the movement posteriorly also allows of a more accurate determination of minor limitations

than is possible with the anterior examination. In a given patient after you have percussed the chest generally and when you wish to focus your attention on the diaphragm movement, you proceed to ask the patient to breathe out and then during expiration percuss downward until a changing note is elicited. A wax pencil mark is placed at this point for reference. After the patient has breathed quietly for a few seconds he is then asked to take a full breath and hold it while percussion determines again the lower border of resonance. A mark is likewise placed at this point. This procedure is repeated several times with the view to accurately checking the preceding observations. It is performed on both sides posteriorly in all patients, and laterally and anteriorly in instances in which one wishes to be especially investigative. The distance between the two marks—*i. e.*, on inspiration and expiration—is normally between 2 and $2\frac{1}{2}$ inches, slightly less in females and in shallow breathers. As a result of percussion studies one also determines the note above and below the diaphragm which is helpful in the differential diagnosis of associated lesions. It is well to recall that the diaphragm may be fixed either in a higher position than normal or a lower position than normal, and in estimating the abnormality of its position its relation to the fixed points on the chest wall and its relation to that of the position of its other half must be noted.

The ***x*-ray examination** is a valuable method for studying the diaphragm, especially by the use of the fluoroscope, whereby we can note its position, the extent of its movement, the rate and the rhythm of its action, and alteration in shadows above and below it indicative of adjacent disease or displacement of associated structures. Although a most valuable adjunct to diagnosis, it must be used only in co-ordination with other clinical methods. It cannot replace them. It is not infallible. It is not always available. It requires experience to interpret. As an evidence of the caution required one might cite Pepper's experience, in which had the exploring needle been introduced at the point in the chest decided upon by the clinician and the roentgenologist, it is probable the bowel contents would have been recovered.

This mortifying experience was avoided only by the sudden death of the patient, and at necropsy the complete, congenital, left-sided diaphragmatic hernia found. Such an event ought to be well-nigh impossible if care is taken in the physical examination and if good fluoroscopic examination together with stereoscopic plates are interpreted by an experienced roentgenologist. Any doubt could be cleared up by the administration of the opaque meal. The discovery of eventration and its differentiation from hernia rests almost exclusively with the roentgenologist.

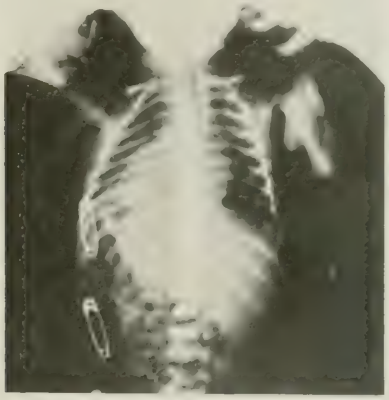

Fig. 121.—Radiograph of a baby only a few days old. Note the high position of the left diaphragm without displacement of the heart. (Eventration of the diaphragm.)

Most of the hernias have been found during life by the roentgenologists. It is a most valuable method in conjunction with other clinical procedures in diaphragm study.

### THE VARIOUS CONDITIONS IN WHICH THE DIAPHRAGM IS INVOLVED

For the purposes of discussion the conditions which involve the diaphragm may be arranged into three principal groups: (1) Those acute lesions which involve the pleural or peritoneal coverings, giving rise to irritation of the diaphragmatic nerves and causing referred pain; (2) those lesions which alter its posi-

tion and interfere with its movements, and (3) the lesion which is associated with an abnormal opening—diaphragmatic hernia.

Group I.—As pointed out in the consideration of the anatomy of the diaphragm, its close relation to the four serous cavities renders it practically always involved when a lesion of the serous membranes lining these cavities occurs in its vicinity; in other words, an acute diaphragmitis is always coincident with a diaphragmatic pleurisy or a diaphragmatic peritonitis. An extensive lesion may involve one diaphragm muscle, and, indeed, often does without involving the other. Let us consider the first of these, namely, *acute diaphragmatic pleurisy*.

**Acute Diaphragmatic Pleurisy.**—As early as 1853 DeMussy pointed out that pain from diaphragmatic pleurisy might occur in the neck and in the hypochondriac regions. Points of tenderness in the latter area are still referred to as "DeMussy's buttons." Now while it is fairly generally conceded that the pleura, like other serous membranes, is non-sensitive, pain does occur when the related muscles become irritated and spasmodically contracted. In other words, the visceral pleura is non-sensitive because of the absence of musculature, while the parietal and diaphragmatic pleuræ are sensitive because of spasm of the intercostal and diaphragm muscles. Capps made some interesting observations on the referred pains from irritation of the diaphragm in cases of pleural effusion. He inserted a stout, metal probe and exerted pressure first on the outer edge of the diaphragm, which produced painful sensations referable to the lower portions of the thorax, flank or abdomen, and then exerted pressure on the central portions of the diaphragm which produced pain in the neck along the borders of the trapezius. The explanation given is that the central portion of the diaphragm is innervated by the phrenic which receives filaments from the third and fifth cervical nerves as it emerges from the neck with the fourth cervical nerve. The skin over the edge of the trapezius is supplied by these cervical nerves. As a result of the irritation of the phrenic nerve in the diaphragm region afferent impulses are conveyed to the cord and disturbances are set up at the origin of the phrenic nerve which are communicated to the other

nerves originating in the neighborhood. The outer portions of the diaphragm are supplied by the lower thoracic nerves and the abdominal areas of pain which occur are in the region of distribution of the eighth and ninth thoracic nerves. Capps reports 93 cases of diaphragmatic pleurisy, 57 had lower lobe pneumonia with pleurisy and 36 had pleurisy alone; 47 occurred on the right side and 35 on the left and 1 case was bilateral. He found referred abdominal pain in 64 cases and the frequency with which abdominal lesions were incorrectly diagnosed is evident by his figures. Appendicitis was incorrectly diagnosed nine times and two cases subjected to operation, cholecystitis was diagnosed in eight instances and two cases subjected to operation, peptic ulcer was diagnosed twice and one case was operated upon, and in various others diagnoses were made of lumbago, kidney stone, abscess of the liver, peritonitis, etc. Referred pain in the neck occurred in two-thirds (62) of the cases and was located usually along the anterior border of the trapezius.

The diagnosis of acute diaphragmatic pleurisy upon local signs is difficult in the absence of the friction-rub which occurs in the involvement of other portions of the pleura. The *x*-ray will often fail. In most instances the presence of a demonstrable basal lesion in the lung is the chief diagnostic factor. Capps calls attention to the frequency of associated pneumonia. I would call attention to its frequency in tuberculosis. Among a large number of tuberculous patients whom I am able to see, both in the Jefferson Hospital Chest Department and in the White Haven Sanatorium, there occur many instances of pain in the abdomen, and I have been guided by the dictum of Webb, Forster, and Gilbert in regard to its interpretation: "*In the tuberculous subject it is especially the part of wisdom to make the diagnosis of one disease fit the different symptoms.*" Among over 1500 cases, the clinical courses of which have been carefully followed, and from a postmortem experience covering several hundred consecutive necropsies, I have had no occasion to regret following this advice.. It is quite true that many abdominal pains are due to actual tuberculous lesions, such as intestinal tuberculosis with localized peritonitis, etc., but those instances

in which an acute appendicitis or other lesion requiring operation occurred, are uncommon and when present are so frank as to be without confusion. Unquestionably, many of the cases of hitherto unexplained abdominal pain in tuberculous patients are due to diaphragmatic pleurisy. The latter pain is seldom likely to be constant at one point, is often present at several points inconsistent with common abdominal lesions, is rarely associated with the same type of board-like rigidity which one gets in abdominal lesions, is unassociated with deep tenderness; may perhaps occur without constipation; does not have certain localizing symptoms, such as jaundice, blood-cells in urine, etc., etc., which we associate with certain intra-abdominal lesions, which are simulated by the diaphragmatic pleurisy. Examination of the diaphragm proper will reveal definite limitation of its movement, as is evidenced by the general or local limitation of expansion, especially in the lower chest—in some instances the breathing assumes a pronounced costal type—the diaphragm shadow may be absent or diminished, the movements of the subcostal angle are limited, especially the costal margin on the affected side.

Acute diaphragmatic pleurisy with effusion, which is usually purulent (loculated diaphragmatic empyema), will be discussed a little further on in the general discussion of fluid collections in the pleura depressing the diaphragm, and diaphragmatic pleurisy followed by adhesions will be discussed also later on in considering high position of the diaphragm.

GROUP II (*a*).—**High Position of the Diaphragm with Lessened Motility.**—This group is typically illustrated by the rare condition known as eventration and very commonly as a result of pulmonary fibrosis with diaphragmatic adhesions. Eventration of the diaphragm is a congenital condition affecting in most cases the left side and characterized by an abnormally high position which is independent of any pressure or pulling factor. It was originally described in 1790 by Petit and there are less than 50 cases on record. The term "eventration" is a misnomer, since no abnormal opening exists. In eventration there is simply a thinning of the diaphragm, the layers remaining intact and the struc-

ture assuming a higher position than normal. In embryonal life the diaphragm originates in the region of the neck and its failure to descend to its proper position is as yet but little understood. Its dependence upon some developmental failure is fairly generally conceded. Its occurrence in the newborn; its association with other congenital anomalies; the involvement of the left side in almost all cases (which coincides with the complexity of the development of the left diaphragm); the hypoplasia of the corresponding lung; the absence of compression of the lung and contiguous structures; the absence of deformity of the chest wall, argue against an acquired lesion, *e. g.*, a high position due to adhesive pleuritis and pulmonary fibrosis. The following are the brief clinical notes of a case of eventration which I reported about one year ago:

An adult female of thirty-nine years, with a negative family and previous personal history, stated that about three months prior to coming under observation she began to have pain in the epigastrium and left lower chest associated with attacks of vomiting. The pain radiated to the back. No constant association of pain with the taking of food could be established. She was referred to me with a diagnosis of gastric neurosis, the *x*-ray having eliminated gastric ulcer and cancer. The physical examination revealed the following: A fairly well-nourished adult female, no jaundice; eyes, mouth, ears, and neck normal. Chest well formed and symmetric, expansion definitely limited on the left side, especially over the lower portion. Apex-beat not visible or palpable. Percussion revealed tympany below the third rib in the anterior axillary line merging with the tympany over stomach below. Posteriorly on the same side the percussion note below middle of scapula was high pitched and resembled the so-called flat tympany. The percussion note over the remainder of the chest was clear and resonant. Breath sounds were everywhere normal except over the area of altered percussion note on the left lower chest, where they were practically absent. During the auscultation of this area a sound suggesting a splash was heard when the patient moved. No coin sound could be elicited. The physical signs suggested a hydro-

pneumothorax, and this was our provisional diagnosis when the patient was admitted to the hospital. The gastric symptoms gradually cleared while the patient was in the hospital. The finding of the high position of the diaphragm was incidental to the *x*-ray study. After learning of the *x*-ray findings I re-examined the patient carefully a number of times, and upon each occasion was able to demonstrate a distinct flaring upon deep inspiration of the costal border upon the affected left side. Several physicians of experience who saw the patient with me afterward were able to verify this observation, namely, the distinct widening of the subcostal angle on inspiration, a widening due principally to greater divergence of the left costal border. In other words, if I had been as careful in my examination before the *x*-ray was taken as I should have been I would have reached a correct diagnosis without the *x*-ray. As a matter of fact, this case served to impress me as no other has since with the need for careful physical examination of the diaphragm.

**High position of the diaphragm as a result of adhesive pleuritis and pulmonary fibrosis** is a very common lesion. The routine use of the *x*-ray has demonstrated its frequent occurrence in every large group of chronic lung patients such as one sees, for example, in a tuberculosis institution. It is oftentimes unsuspected, since it gives rise to few symptoms separable from those due to the actual pulmonary lesion itself. The crippling of the diaphragm is so gradual that the respiratory function is adjusted to the altered conditions. Whenever a special demand is made upon this function, however, as in exercise, the inadequacy of the pulmonary ventilation becomes quickly evident in the dyspnea which follows. Many patients whose tuberculosis is arrested, and perhaps eventually "healed in," have shortness of breath upon slight exertion. This is apparently distinct from a cardiac weakness, as far as we can determine; and cannot be accounted for by the amount of lung tissue involved. A careful *x*-ray study of the diaphragm in this type of patient will often reveal the cause for the shortness of breath—the diaphragm is found distorted in contour, angulated, pulled up, fixed in a high position, immobile or only slightly mobile—all the result of

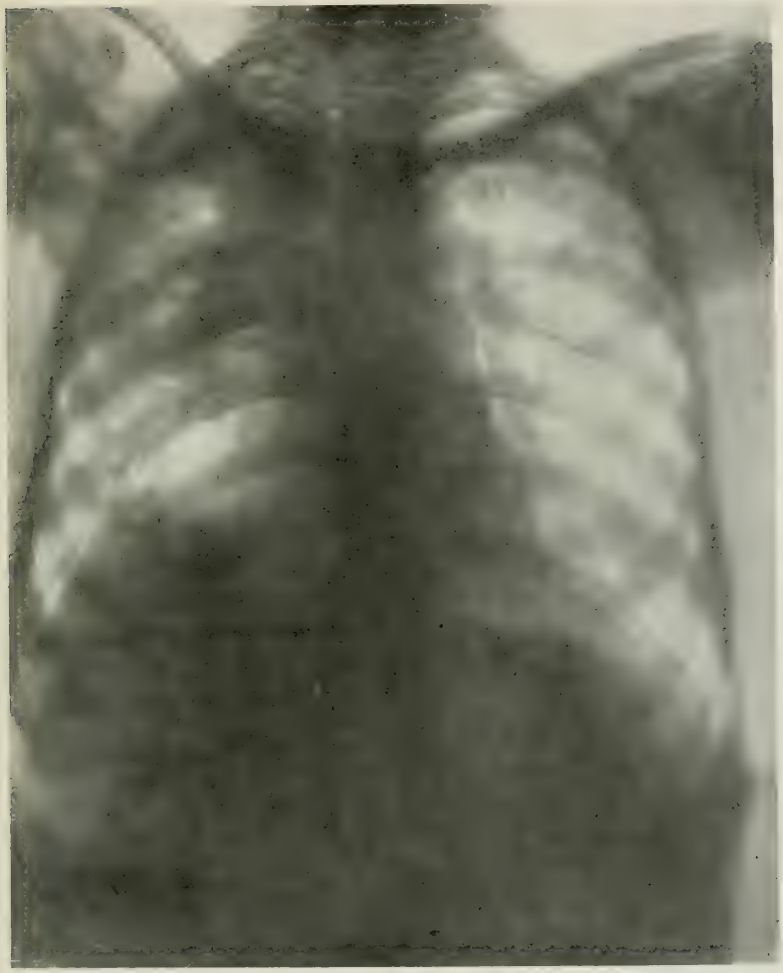

Fig. 122.—Radiograph showing the normal contour of the left diaphragm contrasted with the high position, irregular contour of the right diaphragm as the result of pulmonary fibrosis and basal pleural adhesions. The fluoroscopic examination showed normal mobility on the left side with fixation on the right side. The costophrenic adhesions and pericardiophrenic adhesions obliterate these angles.

contracting fibrous tissue which has glued the diaphragm to the shrunken lung.

**Massive collapse of the lung** is an interesting condition to which Pasteur called attention in 1911, which seems to be in some way related to impaired function of the diaphragm. A part of the lung, usually the lower lobe, or an entire lung becomes airless without any obvious interference with the free entrance of air. The paralysis of the diaphragm from diphtheric neuritis causes a similar massive pulmonary collapse, and it is possible that a variety of influences which directly or indirectly attack the innervation may cause it. During the war not only chest wounds and injuries but injuries at a distance caused occasionally a reflex palsy of the respiratory muscles with varying grades of pulmonary collapse. In civil life it is seen most frequently after abdominal operations. Symptoms may be absent and the condition go unrecognized unless a careful physical examination is made. In other instances symptoms are severe and urgent. Dyspnea, frequent cough, with absent or scanty mucopurulent expectoration are present. The expectoration is never blood tinged. The constitutional symptoms, such as fever, etc., are slight or absent. Both the local and constitutional symptoms may be aggravated by associated inflammatory lesions, such as diaphragmatic peritonitis and pleurisy or pneumonia. The physical signs of massive collapse are those which are ordinarily associated with pulmonary consolidation, increased respiratory rate, lessened movement, dulness, increased vocal fremitus and resonance, tubular breathing, and fine crackling râles. The râles may be absent if collapse is complete. A very striking feature, however, is the retraction of the chest wall, with displacement of the heart toward the affected side and the high position of the diaphragm. The signs upon the opposite side are those of compensatory emphysema. There is an absence of Litten's diaphragm shadow. There is an unequal movement of the subcostal angle—low position of the diaphragm on the unaffected side tending to cause infracostal narrowing, while on the affected side the costal margin is stationary or tends to move slightly outward. If pneumonia develops the physical signs change to those associated with that lesion; the most noticeable being a return of the heart to its normal position, the

presence of a friction-rub, rusty sputum, fever, etc., etc. The *x*-ray is invaluable in showing the high position of the diaphragm and the displacement of the heart and mediastinal structures. It is especially useful in certain difficult cases when massive collapse is confused with pleural effusion, pneumonia, or subdiaphragmatic abscess.

**Subdiaphragmatic abscess produces elevation of the diaphragm** and occurs in two principal clinical forms, the simple or non-gaseous and the gaseous. The simple subdiaphragmatic abscess is more frequently found on the right side and is most frequently the result of an ascending infection from the appendix. Suppuration of the liver, spleen, pancreas, kidney, or, in fact, any abdominal organ may be the primary cause. Infection above the diaphragm may extend through and below, just as subdiaphragmatic infection may extend through and above, producing a simple or suppurative lesion upon the opposite side. It is amazing how few times a serious extension of disease from one side of the diaphragm to the other with implication of the adjacent viscera occurs. This in spite of the fact that the diaphragm itself is practically always involved. Rolleston calls attention to the contrast between the infrequency of the spread of infection from the thorax to the abdomen and the ease with which the spread occurs from the peritoneum to the pleura, as illustrated in the experience of Pitt, who found in 62 cases of streptococcic empyema that 14 spread from the abdomen. A subdiaphragmatic abscess may actually perforate through the diaphragm, producing an empyema, involve the lung, and subsequently empty into a bronchus and be discharged. The symptoms of simple subdiaphragmatic abscess may be absent or overshadowed by the symptoms of the primary focus of infection—an appendicitis, a liver abscess, etc., etc. When symptoms are present they are usually gradual in appearance—chilliness, chills, fever increasing and becoming more irregular, sweats, pallor, increasing leukocytosis with pain in upper abdomen or lower chest, on one or the other side. The pain, as in diaphragmatic pleurisy, may be referred to the neck. Symptoms of respiratory embarrassment may focus attention to possible involvement of the diaphragm.

This structure is usually displaced upward, and if the lesion is on the left side the liver is pushed down. The diaphragm moves very little and the limitation of respiratory movement in the lower chest may be quite obvious. In some individuals with unimpeded costal breathing one may find a slight exaggeration of the "costal flaring" upon the affected side with definite widening of the subcostal angle. The Litten diaphragm shadow may be present, and if so, of value in differentiating intrathoracic conditions. Its *absence* is of no value in differential diagnosis, since an upward pressure of any considerable amount may prevent the diaphragm from "peeling off" on inspection. Percussion from above downward reveals a distinct change in note higher than normal. The upper border of the dulness is more or less fixed, *i. e.*, unchanged by respiration. This is noted especially posteriorly. The dulness merges with the liver dulness and it may be mistaken as an evidence of enlarged liver. The lower border of this organ may be distinctly depressed. Auscultation reveals the same signs as one would expect over a dulness due to a small pleural effusion, or over an enlarged liver pressing upon the lung, *i. e.*, absence of breath sounds and voice sounds with perhaps occasional crackling râles above the line of dulness. It must be remembered, however, that the signs of subdiaphragmatic abscess depend upon its size and position. It may be so small as to give rise to no signs, or very few; or it may be posterior in its location with signs principally in the back; or it may be anterior with perfectly obvious signs, such as local swelling, tenderness, etc., etc. A relatively large abscess just under the dome of the diaphragm and between it and the liver may at times give rise to few signs in proportion to its size. The *x*-ray is valuable in differential diagnosis. It frequently shows minor interferences with the free movement of the diaphragm, as occurs in abscess on its under surface, and shows shadows of deep lesions which it is difficult to determine by physical examination. All methods fail at times, and I recall one instance in which at an exploratory operation a pint of pus gushed forth from above the liver in a patient who had been examined by a skilled internist and a roentgenologist. To differentiate a lesion

above the diaphragm from one below in a patient in whom the signs are equally compatible with a diagnosis of small pleural effusion, or a subdiaphragmatic abscess, one weighs carefully the previous history. In one instance a respiratory disease and in the other some abdominal lesion recent or present may point the way. The movements of the subcostal angle and Litten's diaphragm shadow should be studied with special care. The infracostal narrowing with Litten's phenomena absent favors pleural effusion, while the opposite favors subdiaphragmatic abscess. Hoover considers the phenomena of the subcostal angle as of particular value in the differential diagnosis of subdiaphragmatic abscess, and in 4 cases which came under his observation the costal margin moved outward further and more actively than on the unaffected side. Rolleston refers to two signs which have been employed to decide whether a given collection of fluid is above or below the diaphragm. If the aspirating needle is introduced into a cavity above the diaphragm no movement of the needle occurs on respiration; if the needle passes through the diaphragm the extrathoracic part of the needle moves upward on inspiration and downward on expiration; this is Fürbringer's sign. The second sign is Pfühl's; when the needle enters a subphrenic abscess the manometric pressure and the outflow of pus are greater during inspiration and less during expiration, while the reverse holds good in the case of an empyema. As Rolleston points out, these two signs depend on the normal excursions of the diaphragm being maintained, but this does not always hold good; for example, a pleural effusion may paralyze the diaphragm and so lead to mimicry of the condition in a subphrenic abscess. Further, puncture of the diaphragm may convey infection from the abdomen to the thorax, or vice versa, and is therefore not devoid of danger.

The *second form of subdiaphragmatic abscess* is that in which the abscess cavity contains gas. This form is more frequently found on the left side and is usually the result of a chronic perforating peptic ulcer. Since peptic ulcer is operated upon earlier nowadays than formerly, gaseous subdiaphragmatic abscess has become less common. In a few instances the gaseous

abscess may result from infection with gas-producing micro-organisms. The physical signs in a measure suggest a pyopneumothorax, and for this reason it was termed "subdiaphragmatic pyopneumothorax." The diaphragm, however, is pushed up rather than down. The diagnosis is made upon a careful consideration of the following: There is usually a past history suggesting gastric or duodenal ulceration. The present trouble is often dated to time of sudden onset with pain and symptoms of a localized peritonitis in the upper abdomen. This is followed by the symptoms of suppuration—chilliness, chills and fever, sweats, pallor, increasing leukocytosis, etc. At the same time local symptoms of respiratory embarrassment occur. There is pressure upon the diaphragm. An acute diaphragmitis occurs, and with extension of the inflammation, pleurisy or, rarely, pericarditis, simple or suppurative, may develop. The physical signs vary with the size of the abscess. A large abscess may cause a prominence of the affected side; a unilateral limitation of respiratory movement, especially over the lower part of chest; some prominence in the right upper quadrant due to a pushing down of the liver, or in the left upper quadrant due to the abscess itself; an absence of Litten's sign; tympany above and dulness below which change with the posture of the patient; distant or absent breath sounds with a positive coin test and succussion splash. In a small abscess the signs may be very few. All that one may find are limitation of expansion of the lower chest, presence of Litten's diaphragm shadow, inspiratory widening of subcostal angle due to exaggerated flaring of the costal margin upon the affected side, a higher position with fixation of the lower margin of pulmonary resonance posteriorly as noted upon percussion, no percussion changes due to abscess itself, no abnormal auscultatory phenomena.

In either a large or small gaseous abscess the occurrence of thoracic extension complicates the picture. Pains referred to the neck may occur as in diaphragmatic pleurisy. The differential diagnosis of pyopneumothorax and subdiaphragmatic gaseous abscess is by no means easy. The former often occurs in one who is known to have a pulmonary tuberculosis or in

one in whom there are definite signs of an apical lesion. A previous history of sudden pain, shortness of breath, in one who has had a chronic cough, is in striking contrast to the sudden pain, vomiting, etc., in one who has had a previous history of gastric trouble.

**Paralysis of the Diaphragm.**—Paralysis of the phrenic nerve may be central, peripheral, unilateral, or bilateral. It may be injured by blows and wounds (stab and gunshot), though rarely so. It may be involved in injuries to the cervical cord, as occurs, *e. g.*, in fracture of the spine, or in caries of the spine or cervical spinal meningitis. In surgical operations about the neck it is rarely injured, although I saw it injured once in a surgical operation for the removal of a rather extensive malignant tumor. It may be involved in beriberi, infantile paralysis, and diphtheric paralysis. Its involvement has also been noted in lead-poisoning and in an alcoholic neuritis. Gibson has seen some cases of alcoholic neuritis in which implication of the phrenics, along with the intercostals, has been the immediate cause of death. Paralysis of both phrenic nerves causes complete paralysis of the diaphragm, respiration being carried on by the accessory respiratory muscles. Paralysis of one phrenic nerve involves only the corresponding diaphragm muscle. Symptoms referable to involvement of one phrenic nerve may be slight or absent. Dyspnea may not be apparent if the patient is at rest in bed, or is slight upon exertion. In bilateral cases the interference with respiration may be extremely serious. Much depends upon the ability of the accessory respiratory muscles to carry on the respiratory function. As a result of paralysis of the diaphragm the compensatory action of the external respiratory muscles is seen in the exaggerated costal breathing; the diaphragm shadow of Litten is absent, the subcostal angle is obviously widened upon inspiration; and if one is able to examine the back by percussion, more or less fixation of the lower pulmonary border is found. Auscultation reveals feebleness of the vesicular murmur at the base. The fluoroscopic examination shows clearly the absence of movement. In unilateral cases the lesion may be overlooked. Careful inspection, palpation, and

percussion, with the help of the *x*-ray, when that is available, will demonstrate most cases. Dyspnea may or may not be present. Massive collapse or hypostatic congestion of the base of the lung is likely to occur and simulate pneumonia. In phrenic neuritis the patient may complain of pain in the neck along the anterior border of the trapezius with hyperesthesia of skin in this area.

High position from increased intra-abdominal pressure may occur as a result of ascites, tumors, massive enlargement of any of the abdominal viscera, severe tympanites, etc. In these the lesions are perfectly obvious in their mechanical interference with the diaphragm function.

GROUP II (*b*).—**Low position of the diaphragm with lessened motility** may result from (1) the increased intrathoracic pressure of pleural effusion, pneumothorax, pyopneumothorax, emphysema, pericardial effusion, tumors, etc., etc.; (2) traction on the peritoneal side, and (3) spasm of the diaphragm.

**Pleural Effusion.**—When an effusion occurs in the pleural cavity the fluid gravitates to the level of the diaphragm in most instances. Encapsulated effusions between the lobes and in the upper portions of the pleural cavity do not concern us in this presentation. Effusion at the base may be free or encapsulated and the latter may be small or large, involving any portion of the dome. The encapsulated effusions are usually purulent (loculated diaphragmatic empyema). The effusions are practically always unilateral, although it is well to keep in mind that bilateral effusions occur. The latter are, for the most part, non-inflammatory, the serous accumulations of edema (hydrothorax). The "free" exudates tend to accumulate in the costophrenic sinus, spreading over the surface with the depression of the diaphragm on inspiration and flowing back into the costophrenic sinus upon expiration. This can be demonstrated at times under the fluoroscope. With a small free effusion the intrapleural pressure may still be negative, the lung contracting slightly by reason of its inherent elasticity and the diaphragm movement may remain unimpaired. With a larger effusion the lung is compressed, the diaphragm is depressed, and

the adjacent viscera pushed away (the shifting of the heart and mediastinal structures may in part be due to the pull of the unopposed negative pressure upon side opposite to effusion). The physical signs referable to the fluid and to the diaphragm may be very few in the early stages of the fluid accumulation. Lord states that 250 c.c. in an adult should not escape detection and 100 c.c. in a child may be discovered. Personally, I should say this was rather a low estimate. As the fluid increases the diaphragm shadow disappears, there is a fixation of the movement of the costal margin on the affected side with perhaps inward movement in some cases on deep inspiration. The lower border of pulmonary resonance is higher than normal and rises with the accumulation of fluid. The other signs of free and reasonably large effusion are those which you know as characteristic of effusions, and in most cases the diagnosis is easy, with the *x*-ray very easy, and the exploring needle confirms. However, in small diaphragmatic collections, especially the deep-seated encapsulated effusions, the diagnosis is difficult. These are more often purulent and frequently secondary to definite lung infection, such as pneumonia, etc. The diaphragm structure becomes involved in the inflammatory lesion (acute diaphragmitis). Infection may spread to the peritoneal side. Lord found among 38 autopsies in a series of cases of empyema, peritonitis was present in 9 (7 generalized and 2 localized). Such a lesion may perforate into the peritoneum, externally or into the lung, etc., etc. When small it may give rise to but few signs upon examination. Expansion of the lower chest is generally limited, Litten's diaphragm sign is usually absent, the subcostal angle moves outwardly less than normal or the affected costal margin may be fixed, the lowered position of the diaphragm overcoming the outward movement of the intercostals. The lower margin of pulmonary resonance may be elevated or normal in position, but in either case limited in motion with respiration. The *x*-ray shows a definite shadow above the dome of the diaphragm which is flattened in proportion to the size of the encapsulated effusion.

A most striking illustration of low position of the diaphragm

due to intrathoracic pressure is described in a recent case report by Dr. Riesman of this city. I saw a similar case several years ago in consultation. In both instances there was a massive effusion on the left side with inversion of the diaphragm producing an abdominal tumor. In Riesman's case the tumor is described as "a large, tense, rounded mass, slightly uneven, somewhat tender, and occupying nearly the entire upper left half of the abdominal cavity. Five pints of effusion were withdrawn, and the tumor could no longer be felt." The condition must be a result of great intrapleural pressure with gravity acting as a favoring factor. The diagnosis is not difficult. The presence of a massive effusion, its occurrence on the left side, the character of the tumor which is not like a kidney or spleen, its lack of movement on respiration, the absence of the diaphragm phenomena, the inspiratory widening of the infracostal margin on the left side and fluoroscopic study, point to a correct diagnosis.

I desire at this point to call attention to a phase of the subject which I shall deal with later on, because I do not want you to get the impression that the interference of the function of the diaphragm is purely a mechanical problem. The diaphragm becomes involved in actual disease in many instances of pleural infection, and the resulting crippling is perhaps just as much a result of this as from the mechanical factors. I will explain this in detail when I take up with you the acute and chronic forms of diaphragmitis.

**Pericardial effusion produces depression of the diaphragm** in a striking manner. Hoover states that if the fluid within the pericardial sac is not walled off and lies perfectly free, a considerable amount of fluid, or fluid in sufficient quantities to impede the diastole of the heart, will always give a symmetric narrowing of the subcostal angle during inspiration; and as the fluid is withdrawn the inspiratory narrowing is gradually replaced by inspiratory widening of the angle.

**Emphysema.**—Essential emphysema with chronic bronchitis and the emphysema associated with bronchiolar spasm or laryngeal obstruction are associated with marked depression of the diaphragm with inspiratory fixation or narrowing of the sub-

costal angle. In children with laryngeal diphtheria this phenom-

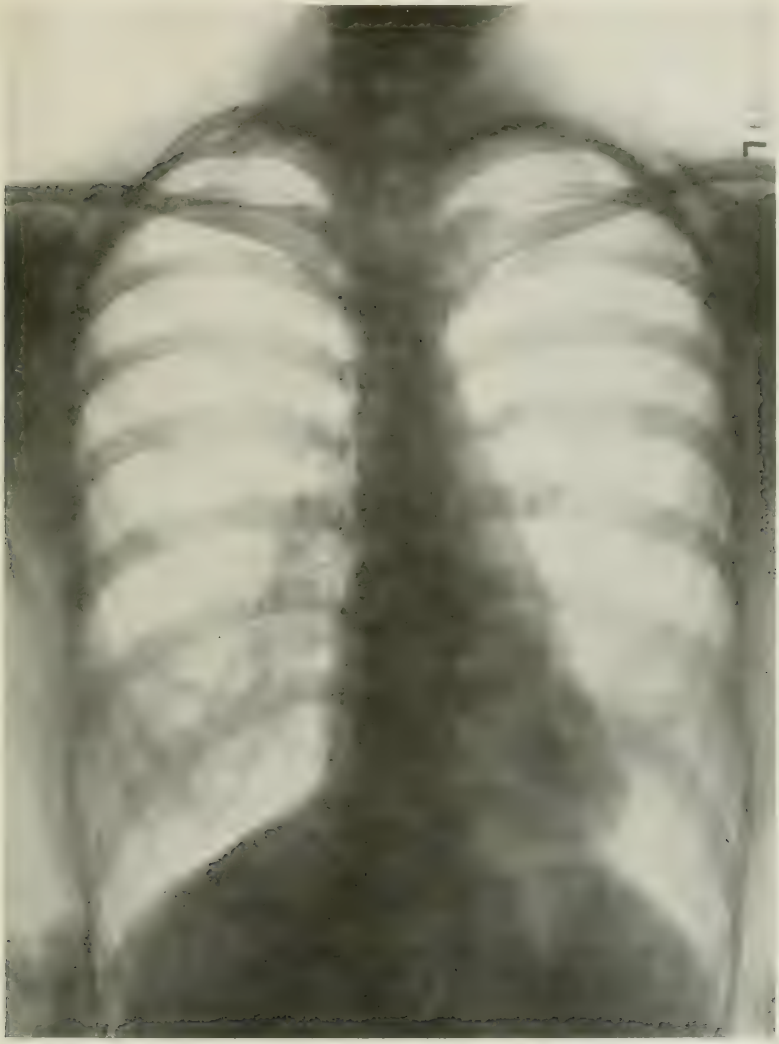

Fig. 123.—Radiograph of a patient with emphysema and chronic bronchitis. Note the low, sloping diaphragm.

enon is often quite noticeable. In bronchial asthma there is a similar overdistention of the lungs with air with depression of

the diaphragm. I have not seen narrowing of the subcostal angle on inspiration in asthmatics, although the greater mechanical advantage of the lower position is evident in the immobility of the costal margins.

Localized vesicular emphysema occasionally occurs as a result of a *foreign body* in the bronchial tree. This is more particularly true of certain organic bodies which do not cast a shadow upon the *x*-ray plate. In a study of a group of these patients Jackson, Spencer, and Manges have been able to localize the foreign body by the acute emphysema occurring in the lung supplied by the obstructed bronchus. The overdistended lung pushes the diaphragm down and the heart and mediastinal structures toward the opposite side. We would expect that a careful study would reveal alterations in the movements of the subcostal angle which would prove of additional value to the other findings in this group of cases difficult to diagnose.

In chronic emphysema of the hypertrophic type the attacks of shortness of breath, with cough and cyanosis which occur, may be related to or associated with a spasmodic condition of the diaphragm. Recently a patient was seen during such an attack, and his diaphragm action was entirely different from that seen previously when he presented the usual signs of large-lunged emphysema. His chest was typical. Litten's sign was absent. The lower borders of the lung as determined by percussion moved but little upon inspiration and expiration. His diaphragm was lower than normal, and yet it apparently did not act to greater mechanical advantage. The movements of the costal angle were apparently normal. This was so startling that I concluded that perhaps the muscle was functionally weakened by disease. I have seen a number of cases of emphysema in old patients in whom this seemed the only reasonable explanation. In others the fixation of the subcostal angle perhaps had some relation to calcification of the cartilages and ankylosis of the costal junctions. However, in the patient mentioned the occurrence of the attack of dyspnea with cyanosis was associated with definite narrowing of the subcostal angle upon inspiration. Previously it had

widened, now it was narrowing. His other physical signs were the same. It occurred to me that what was taking place was a spasmodic action of his diaphragm muscles with each inspiratory effort which enabled the diaphragm to overcome the antagonistic intercostals which it did not do prior to the attack. Or as Hoover points out, the narrowing of the subcostal angle during such an attack may be an evidence of the acute overdistention of the lung resulting from the bronchiolar spasm at the time, the overdistention being sufficient to flatten the diaphragm to a point where it can produce narrowing of the subcostal angle. I have never been able to convince myself that sufficient overdistention of the lung could occur to account for the appearance of such a startling change, especially since the muscle gave all evidences of being weaker than normal. A definite change in the muscle tonus is likewise far from satisfactory, although I believe it is the more tenable of the two theories.

**Low position of the diaphragm due to spasm** probably occurs in tetanus, tetany, strychnin-poisoning, and in the early stages of an epileptic convulsion. Examination of the diaphragm is seldom made in these conditions for obvious reasons. The spasm of the diaphragm in these conditions is seldom as severe and as constant as that involving the voluntary muscles, or else life would be promptly terminated. I have seen instances in which intermittent spasms of the diaphragm of great severity have occurred, and to observe such a patient is to see the sudden checking of breathing for a few minutes with distinct narrowing of the infracostal angle at the height of the spasm.

Clonic spasm of the diaphragm occurring with spasmodic closure of the glottis during inspiration gives rise to what is commonly known as hiccough. It is usually a reflex phenomenon, arising from a great variety of causes which produce an irritation of the pleural nerves and laryngeal branches of the vagus. The attack may be of brief duration or perhaps over many hours and days and produces profound exhaustion. It may be due to some trivial cause, such as indigestion, and the attack passes

off promptly; or it may occur in association with some serious gastric, gall-bladder, or peritoneal lesion. It also occurs as a manifestation of derangement of the nervous system, as a neurosis, *e. g.*, in hysteria; as an evidence of toxemia, *e. g.*, uremia; or in active organic nervous disease, either central or peripheral, *e. g.*, hydrocephalus, meningitis, pressure upon the phrenic nerve by tumors, etc., etc.

Group III.—**Diaphragmatic hernia** may be congenital or acquired, and occurs through one of the normal openings which has become dilated, or through an abnormal opening and is characterized by the protrusion of abdominal contents into the chest cavity. The abnormal opening may exist at birth as a result of a developmental defect, but the protrusion may not occur until some time after birth. Knaggs collected 24 congenital cases, 15 of which were between six weeks and sixty years. In 9 the stomach was the only viscus entering the sac. Acquired diaphragmatic hernia results from penetrating and gunshot wounds, severe blows or falls. The left side is most frequently involved, and as in the congenital form, the stomach is usually the protruding viscus, although liver, intestines, or spleen may do so. The acquired hernia is really an evisceration and should be separated from the true congenital diaphragmatic hernia. The congenital form is apt to be latent as far as symptoms are concerned, while with evisceration there occur the initial symptoms of shock and in some instances sudden death. In those patients who survive, pain, shortness of breath, and vomiting are frequently present. Frequent short, painful cough and hiccough may be present. The signs are not unlike those of pyopneumothorax—prominence of the affected side, usually the left, limitation of expansion, absence of Litten's diaphragm sign, tympany over an area which normally reveals the note of pulmonary resonance, fixation of the lower margin of resonance with respiration, change of position of upper border of dulness with change of position (shifting dulness), diminished or absent breath sounds and voice sounds, coin test positive, and in some instances a succussion splash. The *diagnosis* is made when there is a history of trauma in acquired cases,

oftentimes gastro-intestinal symptoms for some time in the past with attacks of pain, nausea and vomiting, etc., and absence of respiratory symptoms, such as chronic cough and expectoration. Upon physical examination the immobility of the subcostal angle compared to subcostal narrowing as occurs in pneumothorax, the gurgling sounds which are occasionally heard, the variation of the signs depending upon the contents of the stomach, are important aids in differential diagnosis. The *x*-ray examination is quite conclusive, especially when the fluoroscope is used with the opaque meal. The entrance of the bismuth-containing fluid into the thoracic cavity is quite striking. The following case report from the service of Dr. McCrae in this institution, with notes by Dr. Patterson, is highly instructive:

G. D., male, white, aged fifty-one years, was admitted on November 29, 1920. His chief complaint was pain in the upper abdomen after eating. He states that he has always enjoyed reasonably good health. His occupation was that of a machinist and he lost no time from his work, except for one month following an accident five years ago, until about six or seven months ago, when he began to notice "general weakness associated with stomach trouble." His past history shows croup and tonsillitis in childhood, typhoid fever at fourteen years, and a mild attack of influenza during the epidemic in 1918. Five years ago in an accident he was squeezed upon the right side in the mid-trunk between two freight cars. Pain, nausea, vomiting, and weakness occurred. He was able to walk to a nearby automobile, which took him to a hospital, where he remained for one month. At the hospital he was told that he had several broken ribs, but that nothing else was wrong. No *x*-ray was taken. His right side was strapped with adhesive strips. He was in bed about one week and then was up and about until his discharge. After the initial pain subsided he had no annoying symptoms. He returned to work and suffered no annoyance. About one year later he had a mild attack of indigestion of short duration. In March, 1920 he had an acute attack of pain in the pit of the stomach, but with no nausea or vomiting. This

attack likewise cleared up promptly. Since then the attacks of pain have recurred and with shorter intervals between until prior to admission they were quite constantly present one to two or three hours following the ingestion of food. Sometimes the eating of crackers and milk before retiring would help to "keep the pain away" during the nights. His bowels have been regular and he has lost no weight. He has not had nausea, vomiting, cough, expectoration, or dyspnea. The physical examination shows some cyanosis, a short neck, an emphysematous type of chest, resonant lungs with bubbling râles at left base and over left lateral regions. The heart sounds are distant and the cardiac impulse scarcely palpable. The abdominal wall thick, and there is tenderness to the right of the navel. The radial arteries are thickened. The breath sounds over the lower right chest are quite distant and the râles at left base quite evident. Accurate percussion of the heart is difficult because of a very thick chest wall. There is nothing in the physical examination to suggest a diaphragmatic hernia. The movements of the subcostal angle are normal. The Litten diaphragm sign is absent, but this could readily occur normally in one in whom the chest wall is as thick as in this patient. The Wassermann test is negative and the blood, urine, and sputum examinations show nothing of importance. The *x*-ray study showed a rather striking lesion of the diaphragm. Dr. W. F. Manges reported that a hernia of the left diaphragm was present. The sac contained almost the entire stomach in an inverted position and also the hepatic flexure and most of the transverse colon. A considerable portion of the omentum was also present. The opening through the diaphragm seemed rather large and the sac was present mostly in the right thoracic cavity. I saw the fluoroscopic examination with the barium meal and the position of the diaphragm with the stomach above. It was rather a disturbing experience to find such an obviously gross lesion with so few physical signs other than those which one might easily attribute to some thickening of the pleura on the right and congestion of the base on the left—the latter as a result of the obvious myocardial degeneration. The diaphragm open-

ing was probably congenital, since nothing in the past would seem in keeping with an acquired lesion. The history of an injury five years ago was associated with relatively mild symptoms to account for any rupture of the diaphragm at that time. The injury may, however, have caused the stomach, etc., to enter the previously unoccupied opening or forced more abdominal contents into the thoracic cavity. This is entirely possible or the injury may have had nothing to do with the lesion. The patient has been feeling almost well during the past week and wishes to go back to his work. He has been absolutely without pain or discomfort since December 6th until today, December 15th. As you look at him you cannot imagine that beneath his well-nourished outer appearance there is such a gross lesion as a diaphragmatic hernia. This lesion is a rare one, and roentgenologists and pathologists of experience go many years before they see a first or second case among large series of *x*-ray and post-mortem examinations. It is usually overlooked clinically unless the *x*-ray study is made.

**Diaphragmitis, Acute and Chronic.**—So far we have been considering disorders of the diaphragm principally from the viewpoint of a mechanical interference with its movements as a result of adjacent lesions. Active involvement of the diaphragm in inflammatory changes occurs more frequently than we perhaps realize. Histologic studies show an almost constant leukocytic infiltration in the presence of inflammatory lesions in its vicinity. Disorders of function due to disease of the diaphragm must be taken into consideration, in addition to the simple mechanical interference with its movements in the presence of adjacent inflammatory lesions. Active diseases of the diaphragm is not to be wondered at, considering the intimate relationship between the pleural serosa and the diaphragm and the dependent position of the latter which allows more or less constant contact with even very small exudates. The same close relationship exists on the peritoneal side, but most peritoneal lesions are lower down and "free pus" tends to gravitate to the pelvis. Even in such lesions subdiaphragmatic peritonitis and diaphragmitis from lymphatic extension probably

occur more frequently than we think, since we tend to base our knowledge of its frequency upon the occurrence of the rather rare gross lesion, the subdiaphragmatic abscess. The chronic changes—chronic diaphragmitis—which follow the acute contribute as much perhaps to the crippling of this structure as the changes in the immediate vicinity. Acute and chronic lesions of the diaphragm may occur independently of disease in the immediate vicinity. In *trichiniasis* the migrating embryos may lodge in the diaphragm producing a local myositis with subsequent encapsulation of the parasite. In severe cases, especially when the intercostal muscles are likewise involved, marked respiratory embarrassment with dyspnea, cyanosis, and death may result. In *scurvy*, hemorrhage into with rupture of the muscle-fiber of the diaphragm may occur, producing marked respiratory embarrassment—a dyspnea which is independent of any pulmonary lesion. In the early stages of *pulmonary tuberculosis* there is a reflex restriction of its movement (Williams' sign) which may be a protective mechanism like that of the muscular rigidity in appendicitis. In the later stages Landis states that of the 9 cases of acute and chronic pulmonary tuberculosis in which microscopic studies of the diaphragm were made, all of them showed the presence of miliary and conglomerate tubercles; and 2 the evidence of chronic interstitial myositis. *In diphtheria*, toxic changes in the diaphragm, as well as in other muscles, has been described. In many *acute infections* we have reason to believe that the diaphragm, like the heart muscle and the voluntary muscles, may undergo serious degenerative changes. The "respiratory fatigue" during convalescence may be due to weakened diaphragm function as a result of such changes. The shortness of breath upon slight grades of exertion during convalescence from some illnesses which we are prone to ascribe to "weakened hearts" may, in reality, be due to "weakened diaphragms" in whole or in part. Faulty pulmonary ventilation giving rise to rapid respiration, in which the accessory muscles may be called into action, may result from a weakened diaphragm, and it seems just as reasonable to assume such a factor as it does to assume a weakened heart. The "crippling"

of the diaphragm following the removal of pleural exudates has been studied by Pryor. Among 83 patients who gave a history of empyema (47 instances), pleurisy with effusion (16 instances), pleurisy with effusion associated with pulmonary tuberculosis (20 instances) the Roentgen study revealed entire loss of motility in three-fifths of the cases, limited or disordered action in one-fifth of the cases, and function unimpaired in one-fifth of the cases. In the group of patients with a previous history of empyema Pryor found among 31 occurring after the fifteenth year and of which 24 had apparently ended favorably, that there was the surprising total of 26 which revealed complete unilateral immobility. The leaflet of the diaphragm was found, with the exception of several instances, in the low position or below the middle position as seen on quiet breathing. The phrenicocostal sinus was abolished in 34 and the phrenicopericardial angle in 31. The half of the diaphragm was flat except in 4 instances, in which it was notched near the costal surface. The dome or any curve was always absent. The ribs of the affected side were pulled down and inward. Among the 5 remaining cases 3 showed in a minor degree the changes noted above with limitation of movement, while 2 presented normal diaphragm contour and movements equal to the opposite side.

Among 16 children of ages two and a half to eleven years—all of whom had apparently recovered from empyema except one, in whom the fluoroscope revealed an additional collection of pus—Pryor found in 8 instances absolute immobility of the diaphragm on the previously affected side; in 5 instances restricted motion with imperfect dome and signs of adhesion, and in 5 normal movement. From his study Pryor concludes that while the child does not escape the crippling effects found in the adult, the frequency of permanent injury is not so great. In pleurisy with effusion the result, as far as permanent damage to the diaphragm is concerned, is less unfavorable, and yet such damage is strikingly frequent. Among 16 instances Pryor found 9 with complete immobility on the affected side, 1 with slight movement and loss of dome, 2 slightly restricted movement with depressed cap of dome, and 3 normal mobility.

In 10 the costal space was obliterated and in 8 the phrenicopericardial angle was not visible.

In tuberculous patients with pleurisy and effusion, of whom there were 20 (15 incipient and 5 moderately advanced), Pryor found 12 with entire loss of movement in the affected side, 2 had greatly restricted movement with flatness and no dome, 2 limited movement with slight appearance of dome, and 4 comparatively normal movement. The altered configuration as to adhesions was found as previously described. This group of tuberculous patients showed no marked dissimilarity from the non-tuberculous as far as the influence of pleural exudates in the diaphragm; the term "non-tuberculous" is used in the sense of a demonstrable pulmonary lesion. It is probable that both groups were tuberculous as far as the pleurisy was concerned. This work of Pryor has demonstrated the harmful influence of pleural exudates upon the diaphragm. In my experience this has likewise been found to be very frequent. On the other hand, a not infrequent finding, which Prayor does not note, is the higher position which the diaphragm assumes as a result of adhesions in the patients with tuberculosis. The reason for this is the frequent fibroid changes in the lung in tuberculosis. Yesterday a postmortem was held on a former patient of the Chest Department. The left lung was fibroid and shrunken to about the size of a large fist; the diaphragm was pulled up by adhesions to the third rib.

Pryor discusses the influence of adhesions, and while admitting their importance, believes there is room for the contention that they may not be the chief factor in the production of the immobility, and may be found after the diaphragm has become disabled. The appearance after the evacuation of the fluid does not explain the fixation of the diaphragm, since the leaflet is found to be immobile immediatey, or soon after operation. Adhesions, according to Pryor, play a secondary rôle. They may exist and yet motion be undisturbed. The diaphragm becomes thickened from exudate infiltration and fibrosis occurs later. Both promote stiffening with loss of elasticity, especially in the dome of the affected side. Fibrous adhesions between the

visceral and diaphragmatic pleura undoubtedly follow, but actual changes in the diaphragm itself initiate the disturbance in diaphragm function. Perhaps future study may reveal the possible collateral influence of involvement of the phrenic nerve producing an early paresis from this cause and the subsequent inflammatory changes determining its fixation.

In conclusion, I wish to call attention again to the fact that although the diaphragm was known to the earliest of medical writers, and its true action in respiration recognized as early as 1603 by Fabricius, its further study is urgently demanded if we are to become enlightened with regard to its undoubted clinical importance. There is a wide field for research concerning its physiologic properties in health and disease. One of the most important recent contributions upon this subject is by Lee, Guenther, and Meleney. These observers made a comparative study of the general physiologic properties of four skeletal muscles of the cat, the diaphragm, the extensor longus digitorum, the sartorius, and the soleus. They found that when actively stimulated and made to do work the excised diaphragm will work for a much longer period and accomplish far more than the other muscles, even more than all together, before becoming exhausted; it is superior in absolute power and in tendency to summate stimuli; it exhibits a greater tendency then to respond to faradic and chemical stimuli by twitches, more or less rhythmic in character; its greater resistance to fatigue is exhibited in its longer working period and its greater work accomplished before becoming exhausted; it, with possibly some other respiratory muscles, is the last skeletal muscle of the body to submit to the paralyzing action of curare; when the body is subjected to high heat and high humidity all the muscles are affected deleteriously, but the diaphragm is affected far less than the other muscles; by extreme inanition the total working period of the excised diaphragm is shortened far less than that of the extensor, although the total work that can be performed by the former is diminished to a greater degree—a fact that may possibly be associated with the greater activity of the diaphragm. As Lee and his co-workers conclude, the diaphragm is a superior physio-

logic mechanism, and its study opens a wide field for investigation. The immediate clinical need is for some method whereby its efficiency can be determined with an accuracy approaching that of the methods applied in studying the cardiac musculature.

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## CLINIC OF DR. H. R. M. LANDIS

A Clinical Demonstration Given to Post-graduate Students of the University of Pennsylvania

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### ANEURYSM OF THE THORACIC AORTA

This morning I wish to discuss with you the diagnosis of aneurysm of the thoracic aorta. The cases which I will use as a text illustrate most admirably how readily this condition may be overlooked. It is, indeed, a remarkable fact how frequently an aneurysm involving some portion of the arch of the aorta gives but the slightest hint as to its presence, and how the victims will pass from doctor to doctor without any suspicion as to the real nature of their trouble. You must rid your minds of the conception that the recognition of a thoracic aneurysm depends on the presence of a tumor mass which has the characteristic heaving, expansile pulsation, or that in the absence of bulging there is a definite area of pulsation. If one depends on such criteria the great majority of thoracic aneurysms will go unrecognized. Again, it is to be remembered that pulsation is often overlooked because of the failure to adequately inspect and palpate the suspected points at the base of the heart. Carelessness or a faulty technic in the making of a physical examination is largely responsible for errors in these cases.

In addition to these local phenomena it must be remembered that aneurysms act in the same manner as thoracic tumors, and that they give rise to pressure signs and symptoms which may be very slight, or they may dominate the picture. For this reason inequality of the pupils, inequality of the radial pulses, difficulty in swallowing, hoarseness, etc., must always be considered as possibly being caused by an aneurysm.

A carefully taken history and a properly conducted physical examination will go far toward avoiding pitfalls. But even with

the greatest care there are aneurysms, even of a considerable size, which give no clue whatever of their presence. The roentgenologists can furnish many examples of this sort.

### CASE I.—ANEURYSM OF THE ASCENDING PORTION OF THE ARCH OF THE AORTA IN A BOY THIRTEEN YEARS OF AGE

The first case I wish to discuss with you is an extremely rare one. As you know, aneurysms are most frequently encountered in the fourth and fifth decades, although they may occur earlier or later than this. The patient is a colored boy aged thirteen who first visited the Phipps Institute May 3, 1920. He applied for relief because of a "cold" of three weeks' duration. A brother, aged fifteen, has pulmonary tuberculosis; otherwise the family history is negative. He had a slight cough and some whitish colored expectoration. For the past six months he noticed that he was short of breath after exertion. His weight when first seen was 103 pounds; nine months before it had been 110 pounds.

**Examination.**—The first thing to attract attention is an area of pronounced pulsation in the second and third interspaces and extending about 1 inch to the right of the sternum. This pulsation is distinctly felt on palpation, but there is no thrill or diastolic shock. On percussion, the note is dull over this area, extends across the sternum and for $\frac{1}{2}$ inch beyond it. On auscultation there is heard a double aortic murmur, the diastolic portion of which is best heard in the third left interspace near the sternum. The heart is slightly enlarged both to the right and the left.

Two Wassermann tests have been negative. The roentgenologic report from Dr. Pancoast is as follows: "The arch is certainly too wide for the age of the patient. There is a pronounced expansile pulsation, especially marked in the first portion of the aorta. Were it not for the age of the patient I would not hesitate to make a diagnosis of aneurysm." The latter part of this report is interesting as it expresses exactly the opinion in a similar case mention of which will be made later.

**Discussion.**—There does not seem to be any doubt as to the

correctness of the diagnosis in spite of its rarity. The cause of the aneurysm, however, is difficult to determine. The Wassermann is negative and there is nothing in the past history of this lad which throws any light on the condition.

The subject of aneurysm in children and young adults has been admirably reviewed by Bronson and Sutherland (E. Bronson and G. A. Sutherland, Ruptured Aortic Aneurysm in Childhood, with report of case, Brit. Jour. Children's Diseases, Oct.–Dec., 1918) in reporting a personal observation. Their case was that of a child five years and ten months of age with a large fusiform aneurysm which was apparently due to congenital stenosis of the aorta, distal to the aneurysm. They were able to find 7 cases reported in the literature in which the aneurysm was associated with a congenital defect; of this number, 5 involved a patent ductus arteriosus, and in 2 of these death was caused by rupture of the aneurysm. In addition, they found references to 7 cases of ruptured thoracic aneurysm, one of rupture of the abdominal aorta and one of rupture of the thoracic aorta without an aneurysm. Although the skiagram in their case pointed certainly to an aneurysm, it was doubted because of the age of the patient, and the absence of anything in the history capable of producing disease of the aorta. At the autopsy, however, a large fusiform aneurysm was found. In the case under discussion two possibilities as to etiology suggest themselves: (1) That the aneurysm may be the result of congenital lues. It is well known that a study of the aortas of stillborn children has revealed infiltration with mononuclear cells, the presence of spirochetes, and early degenerative changes in a surprising number of these cases. It is quite possible that this may account for the condition in this boy. Against it are the negative Wassermann test and any of the stigmata of congenital lues. In this connection it may be said that Stolkind (Hereditary Syphilitic Aortitis, Brit. Jour. of Children's Diseases, 1920, vol. xvii, Nos. 199–201), who has made a study of the literature, concludes that there is not a single case of proved hereditary syphilitic aortitis in older children, and especially in adolescents and adults, though, he admits, such cases may exist. (2) The

aneurysm may be due to a congenital defect in the aorta, such as stenosis.

CASE II

This man is an Italian, sixty-three years of age, who first came to the Dispensary July 1, 1919. One brother died of tuberculosis and a son is suffering from the disease.

He stated that he had had some shortness of breath on exertion, cough but no expectoration, and slight hoarseness for the past twelve years. His weight at his first visit was 130, and during the next ten months this gradually fell to 120. His pulse-rate was slow and regular.

The preliminary diagnosis, and the one which obtained for nearly a year, was a slight tuberculous infiltration of the right apex. This assumption, however, was based on very flimsy evidence. In the meantime examinations of his sputum proved to be negative for tubercle bacilli. A Wassermann test taken nearly a year after his first visit was strongly positive. He was then given a thorough re-examination. The only tangible clue was an inequality of the radial pulses, the left being much less strong than the right. In addition, dulness to percussion was found both to the right and to the left of the sternum on the level of the second aortic cartilage. There was no tumor, no pulsation, no diastolic shock. The hoarseness and the cough were undoubtedly due to pressure, although at first thought the length of time they had existed seemed against either a tumor or an aneurysm. The roentgenologic examination showed an aneurysm involving both the transverse and descending portions of the aorta.

**Discussion.**—You will recall that Broadbent made a useful classification of aneurysms, namely, those giving rise to physical signs (the ascending portion of the arch) and those giving rise to symptoms (the transverse and descending portions of the arch). The distinction is not, of course, absolute. Generally speaking, it is true that when the ascending portion of the arch is involved, symptoms, especially those arising from pressure, are often entirely lacking, while physical signs (tumor, pulsation, diastolic shock, etc.) predominate. On the other hand, when the aneurysm

involves the transverse and descending portion of the arch physical signs may be entirely wanting or very indefinite, while the evidences of pressure are commonly marked.

This case is probably as good an example as you will ever see of how the initial mistake occurred. In the first place the cause of the hoarseness should have been determined at once. In the next place, if the precaution of examining the pulses synchronously had been taken, the inequality should have instantly suggested aneurysm. Had either of these precautions been taken the diagnosis would have been made nearly a year earlier. It is not pleasant to have such a case pass into the hands of another man more careful in his methods and have him detect what you yourself should have done.

### CASE III

This man is thirty-eight years of age and first came to the Dispensary July 2, 1920. He states that he has 4 living children and that 4 died when but a few days old. His first visit was prompted by what he thought to be a "cold." For the past six weeks he had had a cough, a slight amount of whitish colored expectoration, and some pain in his throat. In addition, he has developed some hoarseness during the past two weeks. His present weight is 145 pounds; twelve years ago he weighed 175 pounds.

**Examination** of his lungs showed nothing abnormal. The only thing that attracted attention to his aorta was a bell-like ringing second aortic sound. As this pointed strongly to an aortitis, the manubrium was percussed and found to be dull. An aneurysm was therefore suspected. The Wassermann was reported strongly positive. The laryngologist reported abductor paralysis of the left vocal cord. The roentgenologist reported a large aneurysm involving the entire arch.

**Discussion.**—You can see and feel for yourselves that there is no evidence of a tumor or pulsation near the base of the heart. The pupils are equal, as are the two radial pulses. The character of the second aortic sound is the only thing that directs one's attention to the aorta. This sound once heard cannot be

forgotten, and is, so far as I know, associated only with disease of the aorta. The sound is difficult to describe. It has been referred to as "clanging," a term Allbutt objects to. Potain refers to it as the *bruit de tabourka*, from its resemblance to the sound produced by an Algerian drum, which is made of an earthen pot with a skin stretched over it. That which comes nearest to describing it is that it is a musical, bell-like sound.

The fact that 4 children died when a few days old, of course, points strongly to syphilis, although not to aneurysm. Again, let me impress on you the importance of hoarseness as a symptom. In this case the hoarseness had been present for only two weeks, while in the previous case it had existed for twelve years. In other words, its long duration in one case and its brief existence in the other could not be used as an argument against aneurysm.

CASE IV

This woman is fifty years of age. Her husband died some years ago of pulmonary tuberculosis. She states that 2 children were still-born and that a third died when three months old. She also volunteered the information that she had had a sore in the vagina years ago.

For the past thirteen years there has been a complaint of intermittent pain in the region of the precordia (substernal pain). For the past two years slight exertion caused dyspnea, and for the past six months she has had a cough and a considerable amount of yellow-colored expectoration.

As you can see from the chest chart made at the time of the first visit, the examiner ascribed her respiratory symptoms to some trouble at the base of the right lung.

Some weeks later she was re-examined, and at this time an inequality of the pupils was noted. The left radial pulse was also found to be weaker than the right. There was no evidence of a tumor or abnormal pulsation. On palpation, there was a distinct diastolic shock felt at the base of the heart to the right of the sternum. On percussion, dulness was noted over the manubrium and for an inch to the right of the sternum. On auscultation a systolic murmur, not transmitted, was heard at

the apex of the heart. Both second sounds were accentuated, especially the aortic. The Wassermann test was strongly positive. The sputum was negative for tubercle bacilli.

A diagnosis of aneurysm was confirmed by the *x*-ray examination, which showed a large aneurysm of the transverse portion of the arch of the aorta.

**Discussion.**—Here again is another case which at first was passed over not only in this dispensary but in several others prior to her coming to us. The diagnosis could have been made at the first visit had the examiner paid heed to the fact that two still-born children pointed strongly to the possibility of syphilis. With this in mind, a Wassermann test, the unequal pupils, and substernal pain should have led to a closer scrutiny of the aortic region. The easy detection of the diastolic shock was almost sufficient to make a diagnosis of aneurysm. Had this been done he would have easily avoided his mistake.

CASE V

The last case which I wish to show you is a young woman of twenty-eight who came to the dispensary for the first time a few weeks ago. Her family history is negative. She has had 4 healthy children and no miscarriages.

The cause of her coming was pain in the epigastrium of one week's duration and habitual constipation. She states, however, that she has had some cough during the night for the past three years. Recently she has suffered from dyspnea on exertion.

**Examination.**—The apex-beat is seen to be displaced slightly to the left, being in the fifth interspace outside the midclavicular line. There is no evidence of bulging of the chest wall or pulsation. On palpation, a thrill, systolic in time, is felt over the base of the heart. Percussion of the precordium shows that the heart is slightly enlarged both to the right and to the left. In addition, there is dulness over the upper part of the manubrium. On ausculation a loud, harsh systolic murmur is heard at the aortic area and over the manubrium. The second aortic sound is accentuated.

Nothing abnormal is found in the lungs or abdomen. The

murmur and the dulness over the manubrium suggested an aortitis or an aneurysm. The Wassermann proved to be negative on two occasions. The *x*-ray report was to the effect that the aorta was decidedly dilated and there was marked expansile pulsation.

**Discussion.**—This case has several points of interest. In the first place, it emphasizes the importance of a thorough examination, as there was nothing in this woman's history to point to her real trouble. The second point of interest is the systolic murmur. It should be borne in mind always that a systolic murmur heard at the aortic area, even if transmitted to the neck and associated with a thrill, does not mean stenosis of the aortic orifice. Such a diagnosis is commonly made in spite of the fact that uncomplicated aortic stenosis is the rarest of the left-sided valvular lesions. Such a diagnosis is justified only when the murmur is associated with a feeble or absent second aortic sound and a slow, retarded pulse. In this case the murmur was plainly not functional in character nor was it produced by stenosis of the aortic outlet. Changes in the aorta itself seemed the most likely inference and suggested the possibility of an aneurysm.

The next point of interest is the etiology. There is nothing in the history nor are there any stigmata pointing to lues. In addition, the Wassermann has been negative on two occasions. The later may prove to be positive after a provocative dose of arsphenamine or the spinal fluid may give a positive reaction. Finally, aneurysmal dilatation of the aorta is not usual at so early an age, although by no means so rare as it is in the earlier periods of life.

## CLINIC OF DR. O. H. PERRY PEPPER

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### MEDICAL ASPECTS OF RETINAL HEMORRHAGE

**(*a*) In Nephritis and Arteriosclerosis: Discussion of Relation of Retinal Hemorrhages to Other Hemorrhages in Nephritis.**

**(*b*) In Anemia: Discussion of Relation of Retinal Hemorrhages to Purpura and Allied Conditions.**

EACH of the patients whose records I will present to you in this clinic exhibits retinal hemorrhages, but, as you will see, these patients represent very varying medical conditions.

A consideration of retinal hemorrhage may seem a little inappropriate for a medical clinic, but I can assure you that the internist, whether or not he carries out ophthalmoscopic examinations on his patients, finds this subject of no little importance. The excellent practical instruction in the use of the ophthalmoscope now being given in many medical schools, and the further opportunities of the intern years have resulted in a growing number of internists adding the electric ophthalmoscope to their diagnostic armamentarium. This group is apt not to be more than moderately skilful in the refinements of fundus examination, and, while easily able to recognize the presence of a retinal hemorrhage, are often unable to appreciate the other evidence by which a trained ophthalmologist might be informed as to the nature of the process bringing about the hemorrhages. Furthermore, internists must know along what lines to investigate a case with retinal hemorrhages who is referred to them for study.

It is important that we remember that a retinal hemorrhage of itself signifies little, and that everything depends upon the etiologic factors at work in the given case. The discovery of a retinal hemorrhage should suggest to the examiner a great variety of possible causes. To emphasize this I have placed on the blackboard (Chart I) a composite list of the causes of retinal

hemorrhage taken from four authoritative works on ophthalmology. A glance will reveal the difficulties of the situation.

CHART I

A. Disease of the vessel wall:
   In the aged, atheroma, angiosclerosis, local retinal or chorioidal disease.
B. Altered composition of the blood, producing or acting with degenerative changes of the vessel wall:
   Pyemia, septicemia, tuberculosis, malaria, recurrent fever, influenza, typhoid fever, ulcerating endocarditis; diseases of the liver, spleen, or kidney; anemia (simple and pernicious), loss of blood, as in metrorrhagia or hematemesis, leukemia, polycythemia, hemophilia, purpura, scurvy, diabetes, gout, carcinomatous cachexia, albuminuria, oxaluria, jaundice, extensive burns of the skin, poisoning with phosphorus, chlorate of potassium, serpent virus.
C. Circulatory disturbances, local or general:
   Embolism or thrombosis of artery or vein. Active or passive hyperemia. Hypertrophy of heart. Stenosis of valves, mitral insufficiency. Suffocation. Compression of carotid. Compression of neck or thorax. Menstrual periods. Whooping-cough. In newborn from pressure during delivery.
D. Sudden alterations of intra-ocular tension:
   Traumatic—as in fracture of skull.
   Operative.
   Glaucoma.
E. Local trauma.

Let us limit our consideration to some of the cases in which the retinal hemorrhages are related to conditions of medical interest. First let us discuss what is probably the most numerous and important group, that is to say, chronic nephritis.

**Case I. M. W. Female, Aged Fifty-one Years.**—Two months ago she commenced to feel tired and weak. These symptoms steadily became worse, and a month ago she developed

nausea, vomiting, and severe headaches. Lately her vision has been failing. These are the salient points in her history.

You will see that she is pale and has the familiar nephritic facies. There is a little exophthalmos. The cardiac dulness is somewhat enlarged and systolic murmurs are heard at both apex and base. The blood-pressure: systolic 245, diastolic 140. In all other respects the physical examination is negative.

The laboratory examinations are as follows:

Blood count, R. B. C. 4,670,000; W. B. C. 10,500; Hb. 81 per cent. Differential count normal. Platelets 348,000 per c.mm.

Urinalysis: Specific gravity 1.010, reaction acid, albumin a cloud. Many hyaline, light and dark granular casts.

Serologic test for syphilis negative.

Phthalein elimination test 10 per cent. in two hours.

Blood chemistry: Blood urea N. 72 mgm. per 100 c.c. Blood plasma chlorids 4.95 grams per liter. Blood plasma $CO_2$ 49 volumes per cent.

In other words, this patient presents all the data necessary to justify a diagnosis of chronic glomerulonephritis. The examination of the eye-grounds reveals an albuminuric neuroretinitis with hemorrhages and exudates. There is marked arteriosclerosis of the retinal vessels.

Before commencing the discussion of this case let me state that almost all of the examinations of the fundus which I shall quote were made or confirmed by Dr. G. E. de Schweinitz, or senior members of his staff, to whom our thanks are due.

In our patient these eye-ground findings were to be anticipated, and they form the usual picture seen in such cases. The hemorrhages here are to be considered as part of the retinitis and not of independent occurrence. Our records will, however, supply us with the details of cases of nephritis with retinal changes without hemorrhages, and others with hemorrhages in the absence of other changes in the retina. This variation in the retinal picture in chronic nephritis is well known to the ophthalomologist, and while the isolated retinal hemorrhage in nephritics is attributed to the rupture of a diseased vessel by the increased blood-pressure, the albuminuric neuroretinitis is

considered largely a toxic phenomenon usually of the terminal stage of the renal disease.

Two factors are recognized,[1] one toxic, the other the hypertension, and it is probable that both may be acting in the production of a hemorrhage. The degree of blood-pressure increase under which a vessel wall ruptures is determined, at least in part, by the severity of the degenerative process in the affected vessel. A healthy vessel wall will successfully withstand high pressure; a diseased one will rupture from even a moderate increase.

On this board (Chart II) I have placed some of the data of a small group of our recent cases of nephritis. I have included the main fundus findings in order that you may compare these findings with the various other aspects of these cases. You will see, for example, that patients with very similar clinical findings have quite dissimilar retinal changes; thus Case 9 in the chart had many hemorrhages alone, while Case 6 had no exudates or hemorrhages, and Case 11 had a typical albuminuric neuroretinitis without hemorrhages.

There has been much discussion concerning the relation of the retinal changes to various phases of the nephritis, but without any very satisfactory results. Attempts[2] have been made to correlate the degree of exudative retinal change with the level of nitrogen retention, and the frequency of hemorrhages with the degree of hypertension. Our cases do not seem to support these contentions, but it should be noted that the acuteness of the nephritic process and, in consequence, of the nitrogen retention in the blood explain the absence of fundus changes in some of our patients with the highest blood urea N. figures. For example, Case 3 in the chart was apparently an acute nephritis of short duration, while in Cases 4 and 8 the history suggests that the marked renal inadequacy had developed suddenly on top of a more chronic condition which previously may not have led to any nitrogen retention. In fact, there seems to be little or no parallelism between the retinal changes and any single alteration in the urine, blood, or blood-pressure.

[1] R. F. Moore, Quart. Jour. Med., 1916–17, x, 29.
[2] Morax and Weill, Ann. d'ocul., 1910, cxliii, 354.

| | AGE | SEX | TYPE OF NEPHRITIS. | CHIEF SYMPTOM. | EDEMA | UREMIC SYMPTOMS. | BLOOD PRESSURE. S. | D. | URINE. Sp. Gr. | ALB. | CASTS. | BLOOD Hb% | R.B.C. | W.B.C. | PHTHALEIN ELIM. IN 2 HRS | BLOOD UREA N. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | 12 | M | ACUTE TUBULAR | EDEMA | + | 0 | 145 | 90 | 1010-28 | TRACE | FEW | 70 | 4950,000 | 6,200 | 67% | 15 |
| 2. | 17 | F. | " DIFFUSE. | COMA | + | + | 143 | 95 | 1004-14 | HY. CLOUD | + | 62 | 3,280,000 | 31,000 | 17.5% | 49.6 |
| 3. | 36 | M | " GLOMERULAR | VOMITING | 0 | + | 200 | 135 | 1022 | LT. CLOUD | + | 60 | 3250,000 | 9,600 | 0 | 142 |
| 4. | 56 | F | CYSTIC KIDNEYS. | UREMIA | 0 | + | 185 | 90 | 1010-12 | CLOUD | + | - | - | - | 0 | 250 |
| 5. | 27 | F | CHR. GLOMERULAR | HEADACHE | 0 | 0 | 215 | 145 | 1005-25 | CLOUD | FEW. | 75 | 4,900,000 | 10,200 | 45% | 15 |
| 6. | 39 | M | ADVANCED " | EDEMA | + | 0 | 186 | 115 | 1007-13 | TRACE | + | 41 | 3020,000 | 12,200 | TRACE | 38 |
| 7. | 23 | M | CHRONIC " | HEADACHE. | + | ? | 160 | 90 | 1009-15 | CLOUD | + + | 80 | 4200,000 | 13,800 | 10% | 113 |
| 8. | 30 | F | " " | MELENA | 0 | + | 175 | 110 | 1012-14 | CLOUD | + + | 25 | 1,400,000 | 10,400 | 0 | 159 |
| 9 | 33 | F | " " | FAILING VISION | 0 | 0 | 240 | 130 | 1.011 | CLOUD | + | 67 | 3400,000 | 7,900 | 17% | 33 |
| 10 | 40 | F | " " | HEADACHE | 0 | 0 | 270 | 150 | 1004-19 | LT CLOUD | + | 80 | 4,560,000 | 7,800 | 55% 35% | 11 |
| 11 | 53 | M | ADVANCED " | DYSPNOEA | 0 | + | 230 | 165 | 1012 | TRACE | + + | 70 | 4,790,000 | 8,100 | 15% | 54 |
| 12 | 49 | F | CHRONIC " | HEADACHE | + | ? | 200 | 140 | 1,013 | CLOUD | FEW. | 65 | 3800,000 | 5,100 | 35% | 37 |
| 13 | 25 | M | CHR. TUBULAR | EDEMA | + | ? | 205 | 125 | 1006-14 | CLOUD | + | 65 | 3920,000 | 8,000 | 17% 30% | 33 |
| 14 | 34 | M | " GLOMERULAR | FAILING VISION | + | 0 | 210 | 140 | 1006-14 | HY. CLOUD | + + | 70 | 4500,000 | 9,100 | 15% | 42 |
| 15 | 20 | M | " " | HEADACHE | 0 | ? | 225 | 160 | 1010-15 | CLOUD | + | 68 | 4,400,000 | 5,400 | 35% | 27 |
| 16 | 39 | M | ADVANCED " | DIM VISION | 0 | + | 230 | 150 | 1010-13 | CLOUD | FEW | 65 | 3,700,000 | 8,500 | 10% | 173 |
| 17 | 15 | F | " " | FAILING VISION | + | ? | 230 | 190 | 1014-26 | HY. CLOUD | + | 66 | 3500,000 | 13,000 | 35% | 21 |
| 18 | 32 | M | CHRONIC " | HEADACHE | 0 | 0 | 195 | 135 | 1,010-14 | CLOUD | + | 76 | 4,000,000 | 7,000 | 40% | 35 |
| 19 | 30 | F | " " | FAILING VISION | 0 | ? | 220 | 125 | 1,010 | CLOUD | + | 55 | 2680,000 | 20,100 | 4% | 69 |
| 20 | 40 | M | " " | HEADACHE | 0 | + | 220 | 115 | 1.013 | HY. CLOUD | FEW | 30 | 880,000 | 16,800 | — | 196 |
| 21 | 22 | F | " " | COMA | 0 | + | 210 | 145 | 1005-18 | + + | + + | 35 | 2660,000 | 8,900 | 30% | 51 |
| 22 | 46 | M | ADVANCED " | HEADACHE | 0 | + | 238 | 138 | 1012-14 | HY. CLOUD | + | 50 | 3.370,000 | 7,900 | 22% | 39 |
| 23 | 17 | M | CHRONIC " | EDEMA | + | 0 | 200 | 130 | 1,010-15 | HY. CLOUD | + | 40 | 2,090,000 | 12,400 | 11% | 89 |
| 24 | 51 | F | " " | HEADACHE | 0 | + | 245 | 140 | 1010 | CLOUD | + + | 81 | 4670,000 | 10500 | 10% | 72 |
| 25 | 43 | M | " " | HEADACHE | 0 | ? | 245 | 170 | 1,007 | CLOUD | + | 60 | 4.700,000 | 16,100 | TRACE | 78 |

T II

| WASSERMANN | FUNDUS EXAMINATION. | OTHER HEMORRHAGIC SYMPTOMS. | RESULT | NOTES |
|---|---|---|---|---|
| — | NEGATIVE. | 0 | CURED. | |
| neg. | EDEMA OF DISCS. | 0 | IMPROVED. | |
| neg | DISCS PALE. VESSELS NARROW | EPISTAXIS | DEATH. | |
| — | NO HEMORRHAGES. NO NEPHRITIC RETINITIS. | 0 | DEATH. | PLASMA $CO_2$ 16 VOLS. %. SOME RETINAL EDEMA |
| neg. | SIGNS OF ARTERIO-SCLEROSIS. | 0 | IMPROVED. | PLASMA $CO_2$ 59 VOLS % AN EARLY CASE. |
| neg. | NEGATIVE. | 0 | IMPROVED. | DIAGNOSIS SOMEWHAT QUESTIONABLE |
| neg. | PRE-ALBUMINURIC RETINITIS NO HEMORRHAGES. | 0 | IMPROVED. | RETINAL HEMORRHAGES CAME 1 MONTH LATER |
| neg. | PROFOUND VASCULAR CHANGES. RETINAL HEMORRHAGES. | MELENA EPISTAXIS PETECHIAE. | DEATH. | COAGULATION TIME - NORMAL. |
| neg | NUMEROUS HEMORRHAGES | 0 | IMPROVED. | LATER HAD NEURO RETINITIS. |
| neg | VEINS DILATED HEMORRHAGES + | 0 | IMPROVED. | DIAGNOSIS ? |
| neg. | NEURO-RETINITIS. NO HEMORRHAGES | 0 | IMPROVED. | |
| neg. | NEURO-RETINITIS. ANGIO-SCLEROSIS. | HEMATEMESIS. | IMPROVED. | |
| neg. | EXUDATES ++ HEMORRHAGES + | 0 | IMPROVED. | |
| neg. | NEURO-RETINITIS. HEMORRHAGES ++ | SEVERE EPISTAXIS. | IMPROVED. | |
| neg. | " " " + | 0 | IMPROVED | TONSILLECTOMY WITHOUT HEMORRHAGE. |
| neg. | " " " + | EPISTAXIS | DEATH | |
| — | " " " + | EPISTAXIS. | DYING. | LARGE TUBULAR ELEMENT. |
| neg. | " " " + | 0 | IMPROVED | |
| neg. | " " " + | HEMORRHAGE FROM LUNG | DEATH. | |
| neg. | " " " + | BLOOD SPITTING | DEATH. | RED CELL COUNT ? |
| neg. | " " " + | 0 | IMPROVED. | |
| — | " " " + | 0 | DEATH | |
| neg. | " " " + | EPISTAXIS | IMPROVED. | |
| neg. | " " " + | 0 | DEATH. | PLATELETS 340,000. |
| neg. | " " " + | 0 | UNIMPROVED | |

The influence of blood-pressure alone in instances of non-nephritic hypertension and in arteriosclerosis is interesting. There seems to be a difference of opinion among ophthalmologic writers as to the frequency of retinal hemorrhage in uncomplicated arteriosclerotic, non-nephritic hypertension. I have here the records of our cases of this condition for the past year or two; in none of the 9 cases were retinal hemorrhages found, although the pressure was over 200 systolic in at least 4 of these cases. Adams,[1] however, describes them as frequent. There is no question whatever as to the frequency of retinal hemorrhages in cases of cerebral hemorrhage or apoplexy. As soon as I turn to the records of these cases frequent examples are found.

**Case II. Arteriosclerosis. Cerebral Hemorrhage.**—C. M. J. Male, sixty-three years of age. Admitted following an apoplectic stroke resulting in coma and hemiplegia. Blood-pressure: systolic 210, diastolic 100. Fundus shows arteries small in caliber, tortuous, and faintly streaked. Several small hemorrhages throughout fundus.

The retina and the basal ganglia are both supplied by end-arteries of the internal carotid and are subject to the same pressure influences. Conditions which bring about retinal hemorrhages in arteriosclerotic individuals with hypertension are apt also to produce cerebral hemorrhages, and this has been shown statistically. Retinal hemorrhages in the arteriosclerotic are warnings of cerebral trouble, and the cerebral apoplexy in the majority of cases follows the retinal hemorrhage within a period of four years.

In these cases also two factors are at work: the degenerative process in the arterial wall and the heightened blood-pressure. There may, however, be no circulating toxin at work as there is in the nephritic cases.

Before we turn to the next type of case with retinal hemorrhage let me discuss for a few minutes the question of other hemorrhages in the course of chronic nephritis, and their possible relation to the retinal hemorrhages. As you know, it is not uncommon for the nephritic, especially the seriously ill nephritic,

[1] Brit. Jour. Ophth., 1920, iv, 297.

to have hemorrhages elsewhere than in the retina. Epistaxis and metrorrhagia are the best known examples, while less common sources of hemorrhage are the lungs and stomach. Hemorrhage into the ear is not uncommon and has been said to be the cause of the tinnitus and partial deafness which are common symptoms in chronic nephritis. The retina and the brain have been mentioned. Conjunctival hemorrhages are not rare. Even generalized petechial skin manifestations have been reported,[1] and to some of these cases the term "hemorrhagic diathesis due to nephritis" has been applied.

The cases abstracted on the chart were selected because of the eye conditions, but they show the frequency of other hemorrhagic phenomena. Five had severe epistaxis; one had epistaxis, bleeding from the rectum, and multiple petechiæ; one had spitting of blood, and another had a definite hemorrhage from the lung. Other recent nephritic cases not included in the chart would add to this list. For example, a girl of fourteen who died in uremia had such marked bleeding from the nose, gums, and vagina that she had been considered a case of purpura and the nephritic condition wholly overlooked.

What relation do such hemorrhagic phenomena bear to hemorrhages in the retina? In most but not all instances retinal hemorrhages are present in the cases exhibiting the bleeding from other sources. It is hard to correlate the two, but it is likely that the same factors bring them about. I have touched on the ophthalmologist's views concerning the causation of retinal hemorrhages in such cases. Let us now consider from a medical viewpoint the question of the causation of the other hemorrhagic symptoms of nephritis.

*A priori* the internist would explain such hemorrhagic phenomena in the course of a chronic nephritis by a diagnosis of secondary purpura hæmorrhagica or of symptomatic purpura resulting from the action of some toxin due to the nephritis. Nephritis is put near the head of the list of the various conditions which cause so-called symptomatic purpura. On the other hand, true purpura hæmorrhagica may develop as a terminal event in

[1] D. Riesman. Amer. Jour. Med. Sci., 1907, cxxxiv, 709.

chronic nephritis, probably as a result of toxic depression of the bone-marrow. Purpura hæmorrhagica, however, reveals itself in a greatly lowered blood-platelet count, and this evidence was not present in the only 2 cases in this series in which platelet counts were made. In one of these patients retinal hemorrhages alone were present, while the other was the girl of fourteen with the severe bleeding from nose, gums, and vagina. Of course symptomatic purpura may occur without any demonstrable change in the blood. In the absence of any explanation on the hematologic side we are brought back to the question of degenerated arterial walls plus hypertension as the cause, not only of the retinal, but also of the other hemorrhages, seen in chronic nephritis. This may prove to be the final answer, for there is no demonstrable fault in the blood; the platelet count is not decreased and the coagulation time is normal (Case 8). If the fault be found to lie in the small blood-vessels, it brings the hemorrhages of the retina in chronic nephritis into closer correlation with the other hemorrhagic phenomena of that disease.

Let me now present as a contrast, examples of another group of cases with retinal hemorrhages.

**Case III. Pernicious Anemia.**—S. V., female, aged forty-six, admitted complaining of weakness, tinnitus, deafness, specks before her eyes, indigestion, tingling in her hands and feet, and mental confusion. Physical examination reveals little other than an intense lemon-yellow pallor. Blood-pressure: systolic 104, diastolic 60.

Blood count Hb. 20 per cent. R. B. C. 550,000. W. B. C. 3840.

Differential: Polys. 63 per cent., lymphocytes 26 per cent., mononuclears 6 per cent., transitionals 1 per cent., normoblasts and megaloblasts and changes in reds characteristic of anemia.

Eye-grounds showed retinal hemorrhages, vessels small, discs pale. Patient died without ever responding to treatment. Autopsy showed nothing save the picture of severe enemia.

This case of pernicious anemia exemplifies this group satisfactorily. Retinal hemorrhages are common in pernicious anemia[1] and may here again be part of a symptomatic purpura or

[1] de Schweinitz, Trans. Amer. Ophth. Soc., 1896.

purpura hæmorrhagica complicating the picture of a severe pernicious anemia.

**Case IV. Acute Aplastic Anemia.**—G. T., male aged thirty-six. Admitted complaining of loss of appetite and weakness. He dated his trouble back to a severe attack of influenza six or seven months previous. Since the influenza he had noticed progressive weakness and dyspnea. Four weeks before admission oozing of blood from his gums commenced and more lately he had several nosebleeds. Physical examination: Marked pallor is obvious; numerous small red petechiæ are present over the body, arms, legs, and eyelids; the edge of the liver and of the spleen can be palpated. The blood-pressure: systolic 134, diastolic 65.

The eye-grounds show very anemic blood-vessels and diffuse retinal hemorrhage.

Blood count: R. B. C. 1,020,000; Hb. 22 per cent. W. B. C. 6500. Differential: Polys. 20 per cent., lymphocytes 80 per cent.

No nucleated red cells, no polychromatophilia.

Patient died on the third day after admission.

Although the total leukocyte count was not so low as is expected in aplastic anemia, and the platelet count was not obtained, yet the other features of the case seem to justify a diagnosis of acute aplastic anemia. In this instance there was not only a purpura hæmorrhagica but also the picture of aplastic anemia testifying to the failure of the bone-marrow to produce erythrocytes, granular leukocytes, or platelets in adequate numbers.

**Case V. Secondary Aplastic Anemia.**—H. N. B., male, aged twenty-eight. Admission complaint: Generalized weakness.

Eight months ago, after working for three months in a dye factory exposed to aniline dye, he developed weakness, dizziness, syncope, tinnitus, and loss of weight.

Physical examination revealed a yellowish pallor; bleeding from the gums and tonsils; purpuric eruption on right arm and later on legs. Blood-pressure: systolic 100, diastolic 30.

Eye-ground examination revealed an optic neuritis with obscuration of all the disc margins and many hemorrhages.

Blood count: R. B. C. 1,720,000; Hb. 23 per cent. W. B. C. 3800.

Differential: Polys. 30 per cent., lymphocytes 54 per cent., large mononuclears 12 per cent., transitionals 2 per cent., basophils 2 per cent. There was no polychromatophilia and no nucleated reds were seen.

The patient improved somewhat under transfusions and left the hospital. He died three months from the date of admission.

In this instance the aplastic anemia with its associated purpura was secondary in type and was due to the chemical poisoning to which he was exposed in the dye-works. It is probable that the harmful substance was paranitrotoluol. Benzol, trinitrotoluene, and similar substances have been frequently reported as producing this picture of bone-marrow failure.

In this group of cases we are again at a loss for an explanation of the retinal hemorrhages. We do not know to what extent vascular degeneration plays a part nor how important the blood changes are. We can see at once, however, that hypertension plays no part in the production of the hemorrhages of this group.

In pernicious anemia, but more especially in aplastic anemia, the blood-platelets are decreased in number, and as a result so-called secondary purpura hæmorrhagica may occur. It is possible that the retinal hemorrhages are part of this picture. However, in severe secondary anemia from intestinal parasites, carcinoma or tuberculosis retinal hemorrhages are said also to occur, and if such cases were truly secondary anemia it is probable that the platelets were not markedly decreased. It is difficult to avoid the conclusion that in this group of anemic cases one must also assume vascular injury by some unknown but "endotheliotoxic" substance acting upon the lining of the smaller vessels. It has been shown that it is by injuring the capillary endothelium that snake venoms and poisons, such as phosphorus and formaldehyd, produce the hemorrhages which are so constant a feature of their poisonings.

It is thought that similar endotheliotoxins are produced by certain bacteria, and it is not impossible that the hemorrhages in anemia are in part due to such a process. It is likely, however, that the altered blood favors hemorrhage directly.

In scurvy and purpura retinal hemorrhages are said to be common, and it is even claimed that they occur in hemophilia. This latter statement seems very improbable as applied to uncomplicated hemophilia; it is much more likely that the hemophiliac only develops retinal hemorrhages as a result of some complication. Severe anemia is a frequent result in hemophilia of the long-continued oozing which so often follows some slight trauma. The development of retinal hemorrhages at such times should be blamed on the anemia rather than directly on the hemophilia.

In the causation of retinal hemorrhages in general several points seem to stand out quite clearly. It would seem that in almost every case there were at least two factors at work. For example, in nephritis the degeneration of the vascular wall does not lead to hemorrhage unless hypertension is also present, and the same is true in arteriosclerosis. Similarly, in anemia the altered blood by itself probably does not lead to hemorrhage unless the vessel wall has undergone degenerative changes.

It is, of course, possible that occasionally one factor may be acting intensely enough to bring about hemorrhages. Thus it is possible that snake venom and some chemical poisons may produce sufficient capillary injury to lead directly to hemorrhage. Possibly there may be sufficient alteration in the blood in certain conditions, especially, perhaps, idiopathic purpura hæmorrhagica, to permit this factor acting alone to produce hemorrhages. I have tried to express this idea crudely in this diagram (Chart III):

CHART III. CAUSATIVE FACTORS IN RETINAL HEMORRHAGE

| Factor I. | | Factor II. |
|---|---|---|
| Changes in vessel wall: | | |
| A. Sclerotic in aged, atheroma | + | Hypertension. |
| B. Degenerative, as in nephritis, anemia, etc. | + | Hypertension or altered blood, or both. |
| C. Degenerative, as in acute infections, etc. | + | Altered blood. |

FACTORS POSSIBLY ACTING ALONE

A. Intense vascular degeneration, as in poisoning with snake venom, etc.
B. Severe alterations in blood, as in idiopathic purpura hæmorrhagica.

If we now turn back to the list of conditions in which retinal hemorrhages occur we will find that, with the exception of those due to circulatory, traumatic, or local conditions, most of the other heterogeneous causes can be interpreted in the terms I have suggested to you. Ulcerating endocarditis probably acts by embolism, as may some of the other infections also. Polycythemia belongs under the heading of thrombosis or of hyperemia. Many of the others may find their explanation in an associated anemia.

It is useless for us to try to reclassify this list of causes, but it is valuable for us to realize that, while there is a multiplicity of separate conditions in which retinal hemorrhages occur, there are certain fundamental influences at work in hemorrhages of the retina just as there are in hemorrhages elsewhere in the body.

There is still much we have not learned about this subject, and when we speak knowingly of purpura hæmorrhagica, diminished platelets and endotheliotoxins, we must admit that these are little more than names, and that there is much more for us to discover.

Apparently the retinal vessels are, so to speak, a "locus minoris resistentiæ" in the matter of hemorrhages from whatever general cause, and it is in this that lies the great value of the early discovery of retinal hemorrhages to the clinician. But this discovery will be of little value unless one is able to distinguish between those hemorrhages due to a local cause, those part of a true retinitis, and those isolated forms due to some systemic condition.

If, however, the type of hemorrhage can be identified and the correct etiology searched out of the many possibilities, then the physician will have gained information which in many instances will be of great value in both diagnosis and prognosis.

CLINIC OF DR. JOHN H. MUSSER, JR.

FROM THE NEPHRITIC CLINIC OF THE MEDICAL DISPENSARY,
UNIVERSITY HOSPITAL

## OBSERVATIONS ON NEPHRITIS

THERE are certain findings in diseases of the kidneys which are not only extremely interesting, but often of great value in diagnosis and prognosis. I want to present to you today some observations that had been made upon 4 nephritic patients and which are rather interesting from several standpoints. I will not take the histories up in detail, but rather will give you a brief outline of each case and at the same time discuss with you the interesting observations that were made on these patients.

### CASE I

The first patient, A. E., was sent to the hospital on account of, what appeared to be, an acute infection of the gall-bladder. Her past history was negative except for syphilis and intensive arsphenamine treatment several years ago. The report of the routine preliminary urine examination from the laboratory showed a cloud of albumin and many granular casts. On the basis of this finding the phthalein estimation was made, which was less than 5 per cent. in amount in the two specimens. After being in the hospital a few days the leukocyte count fell, temperature came down, and all signs of an acute infection disappeared. However, the urinary findings were still indicative of a renal disease. About this time I saw the patient for the first time, and in looking over her chart found that every specimen of urine that had been sent over to the laboratory had a specific gravity of between 1010 to 1012. At this time the patient, except for obstinate nausea and vomiting, was apparently in very

good condition subjectively and was extremely impatient because of being kept in bed. The urine varied from traces to heavy clouds of albumin and contained erythrocytes and casts. Now the interesting thing is that about this time we attempted to give the patient a Mosenthal test meal. The patient, however, on account of vomiting was unable to retain the food. However, we collected the urine at two-hour intervals during the day and three times during the night. The accompanying table shows the complete fixation of the specific gravity in spite of the variation in the amount of urine that was excreted at the various intervals:

| Amount in twenty-four hours. | Specific gravity. |
|---|---|
| 10 A. M., 40 c.c. | 1012 |
| 12 N., 26 " | 1010 |
| 2 P. M., 74 " | 1010 |
| 4 P. M., 75 " | 1010 |
| 6 P. M., 64 " | 1010 |
| 8 P. M., 125 " | 1010 |
| 12 M., 80 " | 1010 |
| 3 A. M., 74 " | 1010 |
| 8 A. M., 28 " | 1010 |

**Discussion.**—The patient showed very little change during the next week until a few days before death, when the urinary output became practically nil. She became unconscious shortly before death. Now this patient at no time appeared sick. The only outstanding symptom that she presented and for which she might have consulted a physician was the persistent nausea and vomiting. Blood-pressure was low, she had no edema, she was passing a fair amount of urine up to two or three days before her death, she did not appear to be sick, she was comfortable in bed, her blood urea nitrogen was 81.84 mg. per 100 c.c., her urine showed the changes of acute nephritis, her phthalein was practically not eliminated in two hours, and there was a complete fixation of specific gravity. In other words, we have the picture of a person with an exacerbation of probably a chronic nephritis which became subacute under the influence of an infection. The infection subsided, leaving behind a renal inflammation. The acuteness of this could not be appreciated except

by the functional tests which were absolutely classic in type. We were enabled to give a bad prognosis on these findings. As to the fixation of specific gravity I have come to believe that this indicates more nearly the severity of the disease than any of the other tests of functional ability of the kidney.

The pathogenesis of the condition affords an opportunity for some interesting conjectures. The patient had had lues with active arsphenamine treatment. Before and after each injection routine urine examinations had been made, all of which were negative. The occurrence of an acute nephritis without previous renal disease, with merely the acute gall-bladder infection as the immediate etiologic factor, is, of course, possible but rather unlikely. Much more probable is it that the kidney was the seat of degenerative syphilitic changes or else as a result of the repeated injections of the arsenic preparation of a chronic inflammatory condition had been brought about which lighted up when an acute infection made its appearance somewhere in the system, the gall-bladder being the responsible agent in this case. Arsenic has a distinct toxic effect on the kidney; perhaps the arsphenamine preparation of this drug does do more harm to the kidney than we realize at present, and the future will show us many patients with kidneys prematurely broken down who have in the past undergone active antisyphilitic treatment.

### CASE II

This is another case of acute nephritis coming on after an acute infection. This small boy, age seven, about the first week of January developed measles. Following measles he had a middle-ear infection resulting in mastoid involvement. About the middle of February he started to pass urine which the parents say was the color of port wine and in rather small quantities. A week after this time he was operated upon for an acute mastoid, and a few days later I was called in to see him for the first time. He had a urine which contained a large number of red blood-cells and which continued so up until the middle of April. During this time frequent urine examination showed much the same thing: tremendous quantity of red cells, albu-

min, occasional casts, and a specific gravity which varied from 1010 to 1025. From a mixed twenty-four-hour specimen thoroughly agitated and then centrifuged on a large high-speed electric centrifuge in a tube about 15 cm. high there would be a sediment of from 4 to 5 cm. deep of red blood-cells. This excessive amount of red cells and loss continued for the number of weeks mentioned above and then ceased abruptly. The child had no other symptoms worth mentioning. He had but slight anemia, nor was his blood-pressure elevated, nor was the quantity of his urine decreased. Since that time the boy has been apparently well. Repeated examinations of the urine have disclosed nothing.

**Discussion.**—I bring in this case to illustrate to you, as in the first place, how it is possible to develop an acute nephritis when there is infection within the body. This patient had measles, six weeks later he developed a middle-ear condition which was apparently responsible for the nephritis. I have several times seen acute nephritis develop in the course of acute tonsillitis and once during the course of a quinsy. This fact is to be borne in mind, to be watched for, and to be guarded against in the treatment of these acute conditions.

In the second place, I want to call attention to the tremendous amount of blood lost as a result of the acute hemorrhagic nephritis, with but little systemic effect. The lowest hemoglobin estimation was 68 and the red cells 3,890,000 per cm. The actively functioning bone-marrow of a small child must have very rapidly compensated for the blood lost.

### CASE III

The third case which I wish to show you is not entirely a case of nephritis, but rather, I should say, a case of functional disorder of the kidney secondary to prostatic obstruction. This patient when first seen complained of difficulty in micturition and incontinence. When he was examined the prostate was palpated as a small hard body; his bladder was found to be enormously distended and he stated that he had this trouble apparently for some weeks. Shortly after this he was catherized and 1700 c.c. of urine were drawn. The catheter was left in until

the following morning, when the patient pulled it out because he stated it made him uncomfortable. During the period of fourteen hours that the catheter was in the bladder there was excreted 61,000 c.c. of urine, which is, as you know, a perfectly enormous amount. A functional test of his kidneys showed a marked disturbance of renal function which was due, I believe, entirely to back pressure from the enormously distended bladder preventing the proper functioning of the kidneys. It would have been very interesting to have estimated his phthalein output during the period when he was passing such large quantities of urine. Unfortunately, it was not done. The most interesting feature of this case is the prompt return of the kidneys to their proper functioning when the back pressure was relieved, and second, the extremely large quantity of urine which was secreted in a very few hours. This patient had no edema which we could demonstrate, and yet within his tissues there was retained fluids which were more than 7 quarts in quantity and which gave us no external evidence of their accumulation. In other words, it seems fair to assume that while we commonly look upon slight edema as the retention of but a small amount of fluid, in all probability there is the retention of a very large amount of fluid before it manifests itself by the symptom we know as subcutaneous edema.

In this case the urinary findings have shown a tendency toward fixation of specific gravity. The specific gravity has varied from 1006 to 1010; albumin has changed from a faint trace to negative. The phthalein test showed as follows: first specimen, 470 c.c., phthalein less than 5 per cent.; second specimen, 240 c.c., less than 5 per cent.; blood urea nitrogen has varied on repeated examinations from 23 to 32 mg. per 100 c.c. of blood; blood-pressure 140–80.

This patient was unable to retain his catheter on account of the discomfort it caused and which was probably due to median bar involvement. Shortly after this cystostomy was performed and the bladder permanently drained. When the patient's phthalein elimination is increased and the associated cystitis has cleared up the surgeons will perform a prostatectomy.

CASE IV

The next case (W. F., age twenty-six) represents a very rapid development of nephritis and shows some of the complications which may occur in the course of this disease. This young man was admitted to the hospital on August 8th with edema of the lungs. This complication cleared up very promptly and the patient was discharged from the hospital in about a week, entirely upon his own request, because he felt so well. At that time his phthalein elimination was 19 per cent. in two hours; his urine showed clouds of albumin, hyaline, and granular casts. He was readmitted again on September 27th with exactly the same symptom—pulmonary edema. This time we were able to study him a little more carefully and secured the following data: urinary excretion varied in amount in twenty-four-hour periods; specific gravity always varied. There was a slight cloud of albumin, many casts. Phthalein elimination was 30 per cent. Blood urea nitrogen varied from 18 to 21 mg. per 100 c.c. and Mosenthal test showed no fixation of specific gravity and but slight retention of chlorids. His carbon dioxid and alveolar air was 25 per cent. and showed a slight tendency toward acidosis. In addition to the changes in his kidney findings we also noted that he had a well-marked anemia, very much enlarged heart, although evidences of chronic nephritis were negative. Eye-grounds were negative. His blood-pressure showed some extremely interesting findings. When I first took it I found systolic pressure 195—with a disappearance of sound in the brachial artery at 185. This seemed impossible, and I thought it was due to some error in my technic. The next day when I took the pressure it was 185, with pulse pressure of only about 10. The following day it was 190–155. The next day it was the same and gradually fell to 165–130. Subsequent examinations were about the same. If this represented true pulse pressure, taken on the first two examinations, it was undoubtedly the highest I have ever seen. I did not record it, because I thought it was due to some error. The person was again discharged from the hospital at his own request about a month later.

The patient was readmitted again in a few days with the signs of edema of the lungs and cardiac decompensation. Laboratory examinations were much the same as on previous admission except for the phthalein excretion, which dropped to less than 5 per cent. Blood urea nitrogen had also diminished. The patient did very well for about two weeks, then he developed, without apparent cause, an extremely severe, sharp pain in his right leg. The pain was paroxysmal and extremely severe, necessitating frequent resort to opiates. The leg was cold and there was an absence of the arterial pulsation for two days and a line of demarcation of the lower third of the leg. It was found necessary to amputate above the knee on account of the beginning gangrene. The patient survived the operation about ten days, when he died as a result of his cardiovascular renal condition. At autopsy there was found: markedly arteriosclerotic kidneys and a mural cardiac clot, an embolus from which had lodged at the bifurcation of the abdominal aorta, completely obstructing the right iliac and femoral arteries, and incompletely obstructing the left iliac.

**Discussion.**—This patient apparently had a symptom which is relatively frequent in the course of nephritis, namely, acute pulmonary edema. There are various theories as to the pathogenesis of this condition. The most likely seems, in brief, to be as follows: The edema which occurs in a nephritic condition is due in part to the retention of salt as a result of the inability of the kidneys to excrete it, and partly on account of the changes in the circulation in the pulmonary vessels produced by the secondary cardiac complications which occur in the course of nephritis. Acute pulmonary edema is often an extremely severe and dangerous complication, and as in this patient produce symptoms of marked shortness of breath, spitting of frothy fluid, etc. The pulmonary edema is not, however, always of this severe degree, but, on the contrary, there are slight degrees which produce very few symptoms; at times nothing except a few physical signs.

The cause of the thrombosis of the femoral artery and thrombus extending up the artery into the iliac and the aorta,

and, as found at autopsy, partly occluding the left femoral artery, is not definitely known. There was undoubtedly a somewhat marked disturbance in this young man's blood circulation, as evidenced by the extremely high pulse-pressure. If the pulse-pressure represents the "head of flow" of the blood, it can be seen that the high pulse-pressure allowed but a very poor "head of flow." In spite of the high systolic pressure the peripheral resistance, as indicated by the diastolic pressure, was so great that it is conceivable that the actual output of the heart was very small, permitting the formation of an intracardiac clot.

CLINIC OF DR. JOHN H. MUSSER, JR.

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## SOME UNUSUAL MANIFESTATIONS OF CEREBROSPINAL SYPHILIS

THE protean manifestations of syphilis are well known to all physicians. Syphilis may involve any organ in the body and it may produce various pathologic lesions at any time after the first and second stages have passed. It is the one great cause of chronic disease of all parts of the body, notably the cardiovascular system and the liver. To show the frequency of syphilis as a cause of chronic disease in its tertiary state as seen in general medical wards, in 1916 I tabulated all the cases that occurred for a period of six months in the medical wards of the Presbyterian Hospital, and found that some 30 per cent. of the cases had positive Wassermanns and manifestations of tertiary syphilis. Syphilis, of course, is one of the great causes of certain diseases of the cerebrospinal system, not only of frank cases of paresis and tabes but also of many irregular and unusual forms of central nervous involvement which we label cerebrospinal syphilis.

I have 4 cases that I wish to discuss with you briefly today. The first 2 are cases of cerebrospinal syphilis with marked acute meningeal symptoms, and the last two exhibit the gastrointestinal symptoms which are sometimes seen in tabes, and which must always be borne in mind when one is considering the possibility of the patient having gastric or duodenal ulcer.[1]

[1] I wish to thank Dr. Joseph Sailer for the privilege of studying these cases.

CASE I

H. C. Age thirty years.

**Chief Complaint.**—Was brought in in a state of coma, unable to talk, unable to help himself in any way.

**Present Illness.**—Patient has been in this condition for several days. People for whom he works state that for the past week the patient has been acting queerly.

He seemed very disheartened and morose. It was impossible to obtain a history that was at all satisfactory in regard to his former habits.

When patient was admitted the stomach was washed out; no evidence of alcohol.

**Past Medical History.**—Patient has history of syphilis and his former doctor said that he had been treating the patient intensively for the last few months. The treatment consisted of potassium iodid and mercurial inunctions. Has received one dose of neo-arsphenamine, 0.9 gm.

**Social History.**—Has not used a great deal of alcohol, according to the history given by his wife. Occupation, worked as a driver for the Newton Coal Co. for a number of years.

**Family History.**—Married. No children.

**Physical Examination.**—Patient in comatose condition, unable to talk. Not conscious of surroundings. Impossible to attract his attention in any way.

*Skull.*—Scalp clean, devoid of scars. Eyes react to light; pupils equal and regular. Ears and nose normal. Mouth: breath exceedingly fetid; no ulcerations; teeth in fair condition. Gums: marked pyorrhea; tongue thick, white coating.

*Neck.*—No thyroid enlargement. Anterior and posterior glands palpable.

*Thorax.*—Symmetric expansion; both sides equal.

*Heart.*—Apex impulse in fifth interspace, slightly outside midclavicular line. Slight impurity of aortic valve sounds.

*Lungs.*—Percussion note normal; auscultation, a few coarse râles at bases of both lungs.

*Abdomen.*—No masses or areas of tenderness felt.

*Liver.*—Edge palpable 1 cm. below costal margin. Gall-bladder, spleen, and kidneys are not palpable.

*Extremities.*—Arms and legs flail-like. Reflexes very sluggish. Kernig's sign negative.

About 10 c.c. of spinal fluid removed. No excess pressure. Spinal fluid only slightly cloudy.

9/11: Patient's stomach washed out. Large amount of greenish, foul-smelling material evacuated. Patient incontinent—urine and feces.

9/13: Patient seems to be more conscious of surroundings; will talk to colored orderly, but refuses to say anything to doctors and nurses.

9/15: Patient seems more willing to talk, and has been taking nourishment better.

9/16: Patient converses fairly well, but seems stubborn, and refuses to co-operate with nurses' orders.

9/17: Patient became wildly delirious and unmanageable, and it was necessary to send him to Blockley.

**Laboratory Examinations.**—9/9: Urine, specific gravity 1032, acid, cloud albumin, no sugar; few hyaline casts; amor. urates; epi. W. B. C. ++; mucus.

9/11: 1024; neutral; faint traces of albumin; no sugar; mucus; few W. B. C. Occ. epi. and hyaline casts.

9/13: Specific gravity 1020; acid; no albumin; no casts; very few W. B. C.

**Blood Examination.**—9/10: Blood urea N. 28.8 mg. per 100 c.c. Wassermann negative.

**Spinal Fluid.**—9/10: Amount 10 c.c., appearance very slightly cloudy, color clear. Pandy +; Noguchi positive; sugar 0. Cells per 1 c.mm., 26. Polys., 10 per cent. Lymph., 90 per cent. Endoth., 8. R. B. C.: Many. Smear—no organisms. Cultures—no growth. Wassermann ++++ with 0.1 c.c.

**Temperature, Pulse, and Respiration.**—In the first twenty-four hours the temperature reached 101° F., pulse 110, and respirations 40. Within the next twenty-four hours the temperature and pulse-rate had become normal or subnormal, where they remained the following forty-eight hours that the patient

was in the hospital. The respirations during this latter period were slightly accelerated.

CASE II

D. C. C. Age thirty-five years. (Patient is comatose. History obtained from friend.)

**Chief Complaint.**—Sleeping for past few days and cries out in sleep.

**Present Illness.**—For past three months patient has not been well. General condition was declining. Chief trouble was with his stomach; unable to eat but little. He has had many copious night-sweats. Strength has been failing and considerable weight has been lost. Has had some slight cough and has spit up blood at different times. Last Monday (Oct. 18, 1920) he began to stay in bed; had violent headaches and was very restless and irritable. Condition progressed. He would lie in a stupor, occasionally uttering a cry or groan. In this condition he was received in the hospital.

**Physical Examination.**—Blood-pressure 135–96. Thirty-five years of age. He is stuporous and does not seem to understand anything. He lies on his back with chin up in the air. The least bit of handling calls forth groans.

*Eyes.*—Lids opened with difficulty. Considerable discharge from them. Pupils were small, equal, regular, and reacted to light. Ears, nose, and throat seemed normal.

No evident paralysis or twitching of any particular group of facial muscles.

Neck showed no pulsations or adenopathy. Neck was rigid and body could be lifted by neck.

*Thorax.*—Rather flat and long. Expansion was fair and equal. Posteriorly, lungs were normal as to percussion note and breath sounds. Over right middle lobe anteriorly moist râles were heard. In left midaxillary line a pleural friction-rib was present.

*Heart.*—Upper border in second interspace, right border at right sternal margin and left border 2 cm. outside nipple line. Heart sounds were regular, of fair quality, and no murmurs. $P_2$ was slightly louder than $A_2$.

*Abdomen.*—Rather flat. No visible peristalsis or tumors. No palpable masses. No areas of tenderness or rigidity.

*Extremities.*—Upper: Reflexes present, equal, but not exaggerated. Lower: Patellar reflexes present, equal, and about normal. No Babinski. Kernig's sign present.

10/23: Patient's condition is unimproved. It is necessary to use restraining strap. Respiration is irregular and more of Cheyne-Stokes' type. Lumbar puncture was done: spinal fluid was clear, but under pressure. Catheterized this morning and 10 ounces were obtained.

10/24: Patient is not improving. Respiration is labored and of Biot type. Rigidity of neck is increased. Patient makes much fuss when moved; cries out as if it hurt to be moved.

Advanced information on the cerebrospinal fluid would indicate a meningitis.

10/25: Patient is still losing ground. Last night heart was very arhythmic, but has calmed down under use of digipuratum. Biot's breathing persisting. Able to take but little nourishment. Colloidal gold curve suggestive of tuberculous meningitis. Blood and spinal fluid Wassermann strongly positive.

10/26: Called at 7.15 this morning, and told that patient's respirations were 12 per minute, while pulse was practically imperceptible. Stimulation failed and he died 7.30 A. M. Autopsy was performed.

**Diagnosis:** Syphilitic meningitis.

**Laboratory Examinations.**—10/22: *Urine*, 1032 specific gravity. Reaction acid; sed. sli. floc., albumin cloudy, no sugar; mic. few W. B. C. Many hyaline casts.

10/23: Blood, R. B. C. 14,350; hemoglobin 82 per cent. Polys., 88 per cent. L. lymphocytes, 2 per cent. S. lymphocytes, 4 per cent. L. monoculears, 3 per cent. Transitionals, 3 per cent.

Blood Urea N. 32.55 mg. per 100 c.c.

**Spinal Fluid.**—Fehling's reduced; Noguchi butyric acid reaction, positive; Pandy, positive. Culture, negative. Wassermann 0.1 c.c. ++++. *Cell count*, 120 per c.mm.; polymorphonuclears, 12 per cent.; lymphocytes, 88 per cent.

**Temperature, Pulse, and Respiration.**—Temperature on admission was 100.8° F. Averaged around 101° F. until shortly before death, when it rose to 104° F. The pulse was persistently slower than the height of the fever would lead one to expect, until twenty-four hours before death, when it first reached a rate of over 100. The respirations became markedly increased only the day before death.

## DISCUSSION

In Case I we have a patient who was brought in in a comatose state. This coma varied from a mild stupor to a dead insensibility, but was not persistent. At times the patient would talk clearly and lucidly, and then again he would become maniacal and wild. His condition at first was suggestive of meningitis, but there were several findings which negatived that diagnosis. He had no eye symptoms, no rigidity, and no Kernig's sign. When lumbar puncture was performed only a small quantity of spinal fluid was removed, not under pressure, and apparently not turbid. The laboratory examinations which were completed some hours later were also very helpful in denying the diagnosis of meningitis meningococcic in origin. The peripheral leukocytes were about normal. The spinal fluid showed quite definite evidence of syphilis; that is to say, a marked increase in the lymphocytes, in the differential count of the cells, a rather slight increase in the total number of cells per cubic millimeter, and, of course, in the very strongly positive Noguchi and Wassermann. Uremia was definitely excluded by the absence of more than a slight increase in blood urea nitrogen. This patient, then, had the signs and symptoms of an acute cerebrospinal disorder. Paresis might have been thought of on account of his history, having had syphilis, but probably would have been excluded because the patient had been mentally clear a week before he entered the hospital. Without laboratory aid the diagnosis could have been made, but not so absolutely and definitely as it was when the findings for the various tests were completed.

Case II is another case which came in with sudden onset of severe headaches, restlessness, and irritability. The patient had

extreme rigidity of neck, Kernig's sign, and in every way was suggestive of cerebrospinal meningitis. The spinal puncture showed fluid under considerable tension, which upon laboratory examination gave very positive evidence of syphilis. The colloidal gold test had a tendency to curve toward the figures of tuberculous meningitis. In this case, again, the laboratory examinations were of immense value. Without them I think it would have been impossible to determine the type of meningitis that was present. There was a discrepancy, however, between this case and the first in the blood examination, as the total number of leukocytes were here increased. There was a marked polymorphonuclear increase as well. At autopsy, as reported by Dr. Eiman, the meninges showed the changes of cerebrospinal lues; the meninges, notably of the cerebrum, showed a congestion with apparently little else, and there was a beautiful syphilitic aortitis. But it was especially interesting to find in the gastro-intestinal tract: first, carcinoma of the intestines which was not yet sufficiently far advanced to produce obstruction, but which probably accounted for the loss of weight and strength that the patient had complained of for some weeks before admission to the hospital. He also had a rupture of an acute ulcer at the cardiac end of the stomach which was probably due to a thrombosis of a small vessel at this end of the stomach and subsequent necrosis. The rupture of this ulcer was undoubtedly of only a few hours' duration.

The next 2 cases illustrate the association of gastric symptoms with cerebrospinal syphilis.

### CASE III

R. G. Age fifty-four years.

**Chief Complaint.**—"Pain in the belly."

**Past Medical History.**—For past three to four months has been having pain in upper left quadrant of abdomen. Pain comes regularly after every meal and lasts about an hour. Any kind of food gives this pain. Pain will sometimes radiate to left scapula. Much gaseous eructations. No nausea associated. No appetite for past weeks. Has to take pills to keep bowels

open. Has lost 42 pounds in weight. Daily becoming weaker and weaker.

No pain, frequency, or urgency on urination. No urethral discharge. No nocturia, no polyuria.

Not subject to hard colds. No cough or bloody expectoration. No pains in chest. Had many nosebleeds at beginning of present illness.

No palpitation or precordial pain. Not dyspneic. Ankles not swollen. Not subject to vertigo. No trouble in walking at night. No shooting pains in legs.

**Past Medical History.**—Typhoid fever in 1900. Had chancre in 1902; treated, and doctor said it was cured. Denies gonorrhea.

**Social History.**—Teamster. Meals and sleeping quarters very irregular. General hygiene has been poor. Coffee in moderation. No alcohol. Tobacco.

**Family History.**—Wife living and well. Six children living and well. One child has stomach trouble. Wife had one miscarriage, next to last baby. Mother living and well.

**Physical Examination.**—Adult male, well developed, about fifty years of age.

*Scalp:* Partially bald.

*Eyes:* Pupils contracted, regular, and react very sluggishly to light, but normally to accommodation.

*Mouth:* Teeth in good shape. Throat not congested. Posterior occipital glands vaguely palpable.

*Chest:* Expansion good and equal. Tactile and vocal fremitus equal. Percussion note resonant and voice and breath sounds normal.

*Heart:* Upper border at upper edge of third rib. Right border 1 cm. to right of midsternal line and left border 11 cm. to left. Apex-beat neither palpable nor visible. Apex sounds are faint, but regular. Aortic second louder than pulmonic second. No murmurs heard.

*Abdomen:* Full, somewhat flat. Flanks bulge. No visible masses or peristalsis. No wave transmission on percussion. Flanks are tympanitic.

Liver dulness extends from fifth rib to 1 cm. below the costal margin. Spleen not palpable. Inguinal glands palpable.

*Extremities:* Upper: Radial pulses equal and fairly easily compressed. Epitrochlears not palpable. Lower: Reflexes at patella equal and prompt. Babinski negative. Blood-pressure, 134–78.

**Tentative Diagnosis.**—Malignancy of upper right abdomen.

*Blood:* Leukocytes 6650. Hemoglobin, 85 per cent. Differential count: Polys., 66 per cent. L. lymphocytes, 2 per cent. S. lymphocytes, 28 per cent. L. mononuclears, 2 per cent. Transitionals, 2 per cent.

Urea nitrogen 17.6 mg. per 100 c.c.

Wassermann, ++++.

*Stomach.*—Fractional curve, essentially normal. *Roentgenograms:* Cow-horn shape, lower border about 1 cm. below the umbilicus. No retention, no filling defect. Cap, antrum, and pylorus appear to be normal.

10/3: **Subsequent History.**—Patient has been on active antiluetic treatment plus correction of dietetic faults since admission to the hospital. His gastric complaints have almost entirely gone, he has gained weight, and his general condition is markedly improved.

10/4: Discharged improved. Directions given as to antispecific treatment.

CASE IV

G. R. Age fifty years.

**Chief Complaint.**—"Pain and gnawing in chest."

**Present Illness.**—Last winter (1919–20) was treated for gastritis. Dieted for weeks and condition apparently cleared up. Symptoms reappeared in May, 1920. Onset was characterized by a burning, gnawing pain in the epigastrium. Pain would come before or after meals; usually an hour after eating, lasting as long as a day at a time. Would wake up at night with pain present. Pain would make him vomit at times. Pain would radiate to precordium. No gaseous eructations. Any article of diet would provoke these pains. Bowels tend to be constipated. Lost about 17 pounds in weight. Strength has decreased greatly.

No pain, frequency, or discharge on micturition. No polyuria or nocturia. No precordial pain except the referred gastric pain. No palpitation. No swelling of ankles. No dyspnea. No vertigo. Not subject to severe colds or severe sore throats. No cough or bloody expectoration. Many years ago had night-sweats.

**Past Medical History.**—Described condition of what was likely rheumatism at age of ten. Not very ill with it. Denies gonorrhea and lues. Vague history of antispecific treatment a few years ago.

**Social History.**—Laborer. Indoor work. Irregular as to meals. Coffee and tea in moderation. No alcohol. Does not smoke.

**Family History.**—Father and mother died of old age. Wife living and well, no knowledge of any miscarriages. Four children living and well. No history of stomach trouble in family.

**Physical Examination.**—Blood-pressure 108–76. Adult male negro of about fifty years. He is fairly well developed, but at present seems quite weak.

*Eyes:* Pupils regular, but right one is 1–1.5 mm. larger than left. Right reacts to light but very slightly, if at all. Left pupil reacts very slightly and sluggishly. Sluggish, but yet positive reflex of accommodation and convergence.

*Mouth:* Teeth, many missing. Tongue protrudes in straight line with coarse tremor.

*Throat:* Normal.

*Neck:* Right posterior occipital glandular enlargement. No pulsations. No thyroid enlargement.

*Chest:* Expansion good and equal except that left apex anteriorly lags behind. Percussion note and breath sounds normal throughout. Tactile fremitus normal.

*Heart:* Upper border second interspace. Right border 2.5 cm. to right of midline and left border 13 cm. to left. Apex-beat not visible, but palpable at upper border of sixth rib 2 cm. outside of nipple line. Heart sounds are regular, no murmurs and of fair quality. Aortic second louder than pulmonic second.

*Abdomen:* Abdomen is flat. No visible peristalsis. No

visible or palpable masses. Slight rigidity and moderate degree of tenderness is found in the epigastrium immediately below the ensiform. Tenderness is in midline. Inguinal adenopathy. Liver dulness extends from fifth interspace to costal margin. Edge is palpable and seems normal. Spleen is not palpable.

*Extremities:* Upper: Radial pulses equal and of good quality. Somewhat hardened. Epitrochlear glands are palpable. Reflexes very prompt and equal. Lower: Patellar and ankle reflexes equal and very prompt. No Babinski.

**Tentative Diagnosis.**—1. Peptic ulcer (duodenal ?) 2. Malignancy (?)

9/28: *Urine:* Specific gravity 1016; reac. alk.; sed. floc. No albumin, no sugar. Mic. neg., few hyaline casts. Cyl. and mucus.

9/29: Specific gravity 1014; acid; no sed., no albumin, no sugar, few hyaline casts.

P. S. P. 1—230 c.c. 10 per cent.
11—470 c.c. 15 per cent.
25 per cent.

*Gastric study: Fractional test meal.*

| Free HCl. | T. A. |
|---|---|
| 18 | 36 |
| 16 | 36 |
| 16 | 36 |
| 16 | 40 |
| 16 | 48 |
| 20 | 50 |
| 15 | 47 |
| 14 | 45 |
| 14 | 48 |
| 20 | 52 |

**Blood Examinations.**—9/29: R. B. C., 4,000,000; leukocytes, 10,700; hemoglobin, 85 per cent.

Differential Count: Polys., 77 per cent. L. lymphocytes, 11 per cent. S. lymphocytes, 1 per cent. L. monoculears, 3 per cent. Transitionals, 8 per cent.

Wassermann +.

10/3/20: Cerebrospinal fluid: Clear; count 45 per c.mm.,

leukocytes. Globulin, positive by Pandy's and Noguchi. Fehling's, marked reduction. Colloidal gold, paresis curve. Wassermann with 0.1 c.c. of spinal fluid: 0.2 +; 0.5 ++++; 1.0 ++++.

10/5: Patient has suffered for past three days with severe, shooting pains, which run from his back around chest and abdomen. Pain caused nausea and vomiting several times. Lumbar puncture done October 3d resulted in withdrawal of 10 c.c. of clear fluid not under pressure. Dr. Eiman reports that it gives a Lange gold curve typical of paresis. Morphin is necessary for pain.

10/8: Given injection of 0.9 grain of neo-arsphenamine yesterday. Very difficult to enter veins. It was necessary to give him morphin last night.

10/10: Much stronger today. Able to eat more food. Pain in arm at site of intravenous, but no infection.

10/11: Patient allowed to leave, but to return to G. U. Dispensary. Result: Improved. Discharged on 10/11/20 and referred to G. U. Dispensary.

**Subsequent History.**—After the lumbar puncture and the first injection of neo-arsphenamine patient's gastric condition improved markedly. He has continued to improve since leaving the hospital under active antisyphilitic treatment.

## DISCUSSION

The last 2 cases represent a condition which is well recognized at the present time and which is appreciated quite universally, particularly by those who have done much work with the late manifestations of syphilis. One of the cases is a typical case of cerebrospinal lues, and the diagnosis could be readily made without the aid of laboratory studies. The other case, however, presented none of the usual stigma of syphilis except the contracted pupils, responding but sluggishly to light. His history was apparently negative, father of a large family, and without the blood reports we probably would not have arrived at the correct diagnosis. However, the laboratory findings and the subsequent improvement on antiluetic treatment showed the

condition was not one primarily of the stomach, but, on the contrary, was due to luetic involvement of the central nervous system.

I have recited the history of these 2 cases in detail, not because they are unusual or rare cases, but, on the contrary, they are cases which are frequently seen and more frequently misdiagnosed. If, therefore, you will bear in mind the possibility of acute gastric pain occurring more or less periodically and associated with normal gastric findings being the result of syphilis, you will make fewer mistakes and achieve better results than if you were to forget this frequent possibility. The Wassermann will often put one on the right track when there is doubt as to the cause of the condition from which the patient is suffering, particularly if it is a condition which is associated with the manifestations of gastric disorder.

## SUMMARY

Four cases of cerebrospinal syphilis are recounted in detail. The first 2 cases are rather unusual evidences of the disease; the last 2 show the frequent finding in the later stages of this widespread disorder.

## CLINIC OF DR. J. P. CROZER GRIFFITH

UNIVERSITY HOSPITAL

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### TYPES OF ANEMIA AS SEEN IN EARLY LIFE

I WISH to talk to you today about some of the varieties of anemia, particularly as they are seen in early life. I have a child here I want to show you; and then, after considering the symptoms, we can determine how well we can fit the case to any of the different forms of anemia which we shall treat.

The patient, L. S., is an Italian male child, born June 20, 1917, and consequently now three years, three and a half months of age. He was brought to the ward on account of his very much enlarged abdomen and his "yellow" color. According to the parents, he has had a bad color ever since he was born, the abdomen has always been large and hard, and he has always been somewhat weak; not walking until the age of two and a half years. He has never had any acute illnesses except occasional attacks of slight fever. The family history is negative, the parents being healthy, and one older sister, aged four and a half years, being perfectly well. Careful physical studies have been made of him, from the reports of which I shall read extracts bearing directly upon the case: The head is large and box shaped, with distinctly prominent frontal bosses, that is to say, a distinctly rachitic head. The mucous membrane of the mouth is very pale; the tonsils are enlarged and ragged. The cervical glands in various parts of the neck are slightly enlarged. The skin of the body is very pale and has a somewhat sallow tint, but without any evidence of jaundice. The chest is distended in the lower portion, evidently with a slight costal flare, clearly dependent upon the large abdomen. There are slight traces of beading of the ribs remaining. The left side is somewhat larger than the right. There is a general diminution of the expansion

on inspiration, but it is symmetric. There is nothing to note in the physical examination of the lungs. Auscultation of the heart reveals a rather loud systolic murmur, heard most distinctly toward the pulmonary area, and most faintly at the apex. There is also a murmur occupying the latter part of the diastole, and running into the systolic murmur mentioned. It is loudest in the apical region. The apex-beat is in the fifth interspace, 7 cm. to the left of the midclavicular line, and the right border of the heart extends 2 cm. to the right of the midsternal line. The abdomen is very prominent, dependent in part upon the gaseous distention, but to a large degree upon the very great enlargement of the spleen. It extends to within 1 cm. of the umbilicus, and downward to $1\frac{1}{2}$ cm. above the pubis. On palpation the spleen is found to be hard, smooth, not tender, with a sharp edge and with a distinct notch. The liver extends 5 cm. below the ribs in the midclavicular line. A study of the urine reveals practically nothing abnormal. Examination of the blood made on admission showed hemoglobin 24 per cent., red blood-cells 2,920,000, white blood-cells 21,800, with 25 per cent. of polymorphonuclear neutrophils, and 67 per cent. of lymphocytes, 1 per cent. eosinophils, and 3 per cent. of basophils. There was also decided polychromatophilia, anisocytosis, and poikilocytosis, but no nucleated red cells. The second examination, two days later, showed hemoglobin 27 per cent., leukocytes 21,600, with polymorphonuclear neutrophils 35 per cent., lymphocytes 58 per cent., myelocytes 4 per cent. A third examination, made yesterday, showed normoblasts, megaloblasts, and a considerable proportion of myelocytes, the exact number of which I have not yet been able to ascertain.

Let us review briefly our findings. The shape of the head and, to a less degree, of the chest points positively to the existence of rickets. The slowness in learning to walk would do so likewise were it not that the ill health from other causes could as readily account for this. The rickets, however, is no longer in an active state. The position of the apex-beat in the fifth interspace points toward an enlargement of the heart, inasmuch as at this age the fourth interspace would be the position in which

the apex-beat is most frequently felt. The existence of enlargement is further proved by the boundary limits which were detailed. The systolic murmur is no positive evidence of an endocarditis. It could as readily be dependent upon an anemia. The presystolic murmur is, however, more uncertain. It is not a common form of anemic murmur; yet I do not feel that this needs to be explained on any other ground. The murmurs are not of the character usually heard in congenital cardiac disease, and I think we can omit this from our consideration. There is decided enlargement of the liver and a very great increase in the size of the spleen. The pallor, as you will note, although suggestive of a faint yellow tint, is not, in fact, this at all. It is rather a peculiar sallow tint, characteristic of many cases of severe anemia, and in this instance aided by the naturally dark complexion of an Italian child. The eyes, as you noticed, showed no icteric tint whatever. The striking features about the blood are the presence of normoblasts, megaloblasts, myelocytes, polychromatophilia, a moderate leukocytosis, a great reduction of the red cells, and even greater diminution in the amount of hemoglobin. It will be noted that although the percentage of lymphocytes exceeds that of the neutrophils, yet that this is quite normal in infancy, and that the ratio which is observed in adult life is only obtained quite gradually as the years pass. The excess in this case, however, is sufficient, I think, to allow us to speak of a slight relative lymphocytosis.

The anemias are usually divided into secondary or primary forms, *i. e.*, symptomatic or idiopathic. The distinction is not a very sharp one. In fact, some anemias are called idiopathic largely because we are unable to assign them to any discoverable cause.

### SECONDARY ANEMIAS

These are produced by practically the same causes as in adult life. These causes may act either suddenly or slowly.

(1) A suddenly acting cause is seen, for instance, in large **hemorrhage,** such as may occur in the newborn from the umbilicus. I have also seen a very rapidly developing anemia with death, the result of hemorrhage into the suprarenal body. Of

course the blood does not stay here, but bursts quickly into the peritoneal cavity, where a large amount of it may be found. There is a disorder entitled the hemorrhagic disease of the newborn, in which bleeding may take place from almost any part of the body. This condition is a more slowly acting producer of anemia. Another slowly acting cause is hemorrhage dependent upon the presence of hookworms, acting usually in older children. Anemia due to hemorrhage is seen likewise, for instance, in intestinal ulceration from typhoid fever or other disorder; and I recall one very remarkable instance of intense anemia, supposed by one physician to be of the pernicious type, which was finally shown to be due to intestinal hemorrhage, and in which autopsy revealed abscess formation and ulceration in Meckel's diverticulum.

(2) **Debility** may be another producer of anemia in early life, and of this there may be various diverse causes. Rickets comes in this category as a prominent factor, very many children with rickets tending to be distinctly anemic. In this little boy we clearly have rickets, but his degree of anemia is away beyond what rickets by itself ought to produce, and we cannot attribute it in this instance to the existence of rickets. Sometimes children are born with congenital asthenia, too weak to get along at all, or in any event very prone to be debilitated and anemic. In fact, as some recent writers have emphasized, there seems often to be a congenital inability of the blood-forming organs to functionate properly, and this probably accounts for the existence of anemia in infants in many instances, in spite of what appears to be good food and good care. Among other causes in this class may be mentioned defects in hygiene and diet; chronic intestinal diseases; persistant loss of albumin, as seen in chronic suppurative processes or in nephritis; and chronic heart disease. This last produces an anemia in children, which, although not often of extreme degree, is yet very decided, and one of the most difficult to relieve.

(3) Next, and last, in the class of the causes of secondary anemia are the **toxic** or **infectious agents.** It is not always possible to make a sharp distinction between the two. These

sometimes produce very great anemia. The various infectious fevers, but more especially malaria and diphtheria, may bring about a very severe degree of it. I saw one little patient some years ago suffering from diphtheria, followed promptly by an extensive purpura, with a hemoglobin percentage, as far as it was possible to make it accurately, of only 10. Among the chronic infectious diseases are to be mentioned tuberculosis and syphilis.

**Symptoms.**—In the cases of suddenly occurring hemorrhage there are produced the rapid development of syncope, extreme pallor, and other similar manifestations, such as are seen in adult life. In the large majority of cases of anemia, however, the hemorrhage is not sudden if the cause is, indeed, hemorrhagic at all, and the symptoms come on slowly, because the agent is a more slowly acting one. There is pallor, but the degree of this does not necessarily indicate the actual degree of anemia. Only an examination of the blood can make the diagnosis sure. Children often appear pale, in whom, in reality, there is no anemic condition. The amount of fatty tissue is not necessarily diminished. In fact, the children may even look plump. They become tired very easily, are disposed to be fretful, or in severe cases are very apathetic. I recall a little fellow four years of age who was brought to my office some years ago with a secondary anemia. That the condition was secondary was proved in part by the absence of any discoverable cause, and still more by the fact that after appropriate treatment he recovered completely. His hemoglobin percentage, however, when first seen was only 15, with the red corpuscles 1,356,000. The little boy was too feeble to walk, and had to be carried into the office. When placed in a chair he sat perfectly still, entirely apathetic, and appearing, as indeed he was, too tired to do anything. Gastro-intestinal disturbances are prone to be present, and there is shortness of breath on exercise if the anemia is decided. Cardiac murmurs are frequently heard, as in this case. These murmurs are, of course, not characteristic of any one form of anemia. There is cardiac dilatation, often a venous hum, and sometimes slight enlargement of the spleen. These symptoms, too, are seen in

any severe case of anemia. As to the blood, there is nothing absolutely characteristic about it in this form of the disease. There is a diminution in the number of the red blood-cells, and one still greater in that of hemoglobin; yet the difference is not very great, the color-index not being very decidedly affected, although slightly lower than normal. The red blood-corpuscles are variously altered in size and shape, and when the anemia is severe there is poikilocytosis and anisocytosis, as in other forms of severe anemia, and a few normoblasts, megaloblasts, and megalocytes may be present. There is some question about the resistance of the corpuscles to hypotonic salt solution, but it would appear to be decreased. The leukocytes are generally unaffected in number.

The question now arises whether this boy is a case of secondary anemia. Do the symptoms which he exhibits fit into this category? I should say that they do not. In the first place, we cannot find any cause; although this, of course, is no positive proof, since one might exist without our having been able to discover it. Further, we find an enlargement of the spleen which is way beyond that which we would expect to encounter in any case of secondary anemia. The presence of rickets, it is true, does tend to be accompanied by some enlargement of the spleen, but, again, not at all to the degree which we see here. His color-index is rather lower than we would expect to find in most cases of secondary anemia, but this of itself would not be sufficient to make any other diagnosis. Take it all in all, especially in view of the great enlargement of the spleen, I think we are forced to the conclusion that his case should be placed in the primary class.

### PRIMARY ANEMIAS

(1) **Chlorosis.**—It may seem odd to you that I should speak of chlorosis at all in this connection. We are prone to regard this disease as one characteristic of females at or past the time of puberty, with which we therefore would have nothing to do as pediatrists. This is, however, not absolutely true. As far as the blood-picture goes, we certainly have a condition of chlorosis, or of chlorotic anemia, not infrequently occurring in

infancy and childhood. That is to say, there is a comparatively slight reduction in the number of red cells, but a great one in the amount of hemoglobin, giving a color-index which is lower than in any other disease. Such cases were repeatedly reported by earlier observers, and even quite recently several articles have appeared in medical journals showing the existence of this chlorotic condition of the blood in quite early life. The symptoms in adult life are very characteristic. I cannot now take time to enter upon them here. In early life they are not so well marked for various reasons, and we must depend upon the examination of the blood.

Could our case by any possibility be placed in this class? The blood-picture is absolutely against it. There is an increase in the leukocytes and too great a diminution in the number of erythrocytes to allow this condition to be called chlorosis. There is also too much alteration in the color, variety, and form of the red cells. Further, apart from the blood, great enlargement of the spleen is not a characteristic of that disease.

(2) **Pernicious Anemia.**—This form of anemia does occur in childhood, but is rare. In infancy it is very uncommon. It has been estimated by a writer whose contribution appeared in the year 1915 that up to that time less than 10 well-authenticated cases had been contributed to medical literature. I have, however, seen it in at least one instance, while in others the blood-picture was extremely suggestive; and I am convinced that the disease does occur oftener than these figures would indicate. The disease is a typical hemolytic anemia, in which the red blood-corpuscles are destroyed to a large extent, and the hemoglobin consequently set free. I will pass around this class microscope in which is placed a slide showing a section of the liver of a case of pernicious anemia occurring in an adult. The section has not been stained, but was merely treated with a solution of ferrocyanid of potassium. You will notice the remarkable blue coloration in the outer and middle zones of the cells of the hepatic lobule, caused by the formation of Prussian blue through the action of the ferrocyanid upon the unduly large amount of blood-iron which is deposited in these cells in this disease.

In the blood of pernicious anemia we get a picture different from that seen in almost any other disease, showing a high color-index. There are normoblasts present and a high percentage of megaloblasts. The red cells are altered in other respects, showing poikilocytes, microcytes, and macrocytes. There is, however, a reduction in the number of leukocytes. A few myelocytes may be found. As to the other symptoms, we have those which are observed in any form of severe anemia, such as the existence of cardiac murmurs, cardiac dilatation, dyspnea, faintness, etc. In children there is sometimes a moderate enlargement of the spleen. In addition to these there is a decided tendency to hemorrhage from the skin and the mucous membranes and an increased resistance of the red cells to hypotonic saline solution.

Can our little patient be called an instance of pernicious anemia? We can, I think, promptly rule him out of this category, partly on account of the very great enlargement of the spleen, partly because of the presence of decided leukocytosis, partly because he has a low color-index, and partly because the resistance of his blood to hypotonic salt solution is normal.

(3) **Aplastic Anemia.**—This need hardly be mentioned except for the sake of completeness. Only a few cases have been reported as occurring in early life. Its chief characteristic is that, while it presents the symptoms of pernicious anemia, and is perhaps a form of this disease, or closely allied to it, the blood-picture shows no effort whatever on the part of the organism to reproduce the blood-cells. The leukocytes are even lower in number than in pernicious anemia, and there is no evidence in the study of the red blood-cells of the production of any imperfectly formed elements such as would be shown by polychromatophilia, anisocytosis, and the occurrence of normoblasts and megaloblasts. We can rule out our case immediately, then, from this category. In every respect it is unlike it.

(4) **Pseudoleukemic Anemia.**—This affection is often called von Jaksch's disease, having been described by him under the name of "anæmia infantum pseudoleukæmica." It is a form of anemia which I wish to consider quite seriously today, because

our little boy looks very much as though he were an instance of it. It is not at all an infrequent disorder. It occurs oftenest in the first two years of life, seldom beginning before the age of six months or after that of three years. Our little patient, although now over three years of age, has been ill quite a considerable time. Very many writers, perhaps the majority, do not believe that it can well be considered a distinct disorder: and this is my own opinion. It probably includes a number of other conditions, some of which are abnormal pernicious anemia, others irregular forms of leukemia, and others forms of secondary anemia. It should be remembered in this connection that the primary anemias and allied diseases in early life are very prone to run an irregular course. Sometimes it has almost seemed as though one disease changed into another as time passed. I recall one child under my care a number of years ago who had repeated examinations of his blood made, all of which, together with the symptoms, indicated that he was an instance of pernicious anemia, and apparently a very typical case. As time passed, however, it was interesting to observe that his blood-picture changed into that of a leukemia, and he died of this disease. In fact, one writer designates pseudoleukemic anemia as the infantile form of a myelocytic leukemia. Other writers have denominated it "rachitic splenomegaly."

When you come to consider the *cause* of this affection, it is easily perceived that it is not well understood. Syphilis has been assigned as a factor. Our little boy, however, has a negative Wassermann reaction, so that at least in this case this cause can be ruled out. The disease has also been attributed to rickets, and it is perfectly true that nearly all the cases do exhibit rickets. Our patient has rickets; but consider for a moment the large number of children with rickets who do not suffer with this grave anemic condition. Some other cause must be operative. It is true that both rickets and syphilis would give enlargement of the spleen, but rarely to the extent seen in this case, and not with the complex of symptoms in other respects which he exhibits. The disease has also been attributed to digestive disturbances or toxic conditions arising from the digestive tract, but of this

there is no certain proof. There may be some constitutional tendency present before birth which interferes with the proper action of the blood-making organs. As a matter of fact, we really do not know what the cause is.

As regards the *symptoms*, the onset is slow, with the gradual development of anemia with a so-called "icteric" tint, which, however, as I said, is not truly an icterus. The children are apathetic or fretful, and suffer from various nervous disturbances. The gastro-intestinal tract is likely to be disordered. There are the other symptoms characteristic of any severe anemia, such as cardiac murmurs and dilatation, as well as dyspnea if the child is old enough for us to be able to determine the existence of this. Edema is not uncommon, usually limited to the extremities. This boy has shown a slight tendency to edema. There is generally no fever. It is true that this patient has had some fever, or oftener a subfebrile temperature; but this is probably due to the presence of some complicating disturbance and not to the disease itself. Further examination of a case of this disorder reveals a very marked enlargement of the abdomen dependent chiefly upon a great increase in the size of the spleen, which extends often down to or below the crest of the ileum, and as far as the umbilicus or even beyond it. It is smooth, hard, not tender, with a sharp edge, and with the characteristic notch. The liver is also, as a rule, somewhat enlarged, but to a less extent than the spleen. There is tympanitic distention of the abdomen in addition to that dependent upon the splenic hypertrophy. This is caused by the existence of rickets.

As to the blood, there is no absolutely pathognomonic picture, although there is in so-called characteristic cases one which is very striking. There is, namely, a reduction in the number of red blood-cells exceptionally down to even as low as 1,000,000 corpuscles, while the hemoglobin diminishes greatly, in severe cases even to 30 per cent. or lower. That is to say, there is a very distinct low color-index, just as this boy exhibits. The red blood-cells show great variation in size and appearance, there being megalocytes, microcytes, poikilocytes, and polychromatophilia. A very striking feature is the presence of a decided num-

ber of normoblasts and megaloblasts. The leukocytes are always increased in number, often up to 50,000, or sometimes more. There are nearly always a considerable number of myelocytes. The chief characteristic of the blood consists, then, in the reduction in the number of red cells, a still greater reduction of hemoglobin, the presence of a decided increase of leukocytes, and the occurrence of altered red cells, nucleated red cells of different sizes, and of myelocytes.

The course of the disease is slow, but the prognosis is by no means always bad. It has been estimated that about 25 per cent. die of some intercurrent disease. There are instances reported which are said to have changed into leukemia; but these were very probably such from the beginning.

What elements, now, are there in the history of our patient which would cause his case to be classed as one of this disease? First of all there is his age, which would tend to exclude leukemia and place him in the category of pseudoleukemic anemia, unless we can advance positive proof that he is an instance of the former affection. Next there is the very great enlargement of the spleen, which would make him an instance either of pseudoleukemic anemia or of myelocytic leukemia. The enlargement of the liver would occur in either affection. Finally, as to the blood, we have in favor of pseudoleukemic anemia a very great reduction in the number of red cells and of hemoglobin, the presence of nucleated red blood-cells, both normoblasts and megaloblasts, the occurrence of polychromatophilia, poikilocytes, and macrocytes, and the presence of myelocytes. If this child is suffering from leukemia, by this time we surely ought to have a greater number of white blood-corpuscles than are actually present, and we should not have such a reduction in the number of red cells and of the proportion of hemoglobin. A degree of anemia such as this boy shows ought to come only in the advanced stages of leukemia, and in that case should, as I said, be attended by a great increase of the white corpuscles. All these features point distinctly toward a pseudoleukemic anemia. There is only one characteristic lacking, and that is a very important one. I was informed this morning that the last

examination of the blood showed a very decided increase in the number of myelocytes. This would point distinctly to a myelocytic leukemia. I do not know, however, just how high we could fix the proportion of myelocytes in the blood in cases of pseudoleukemic anemia before we should be obliged to give up the diagnosis of the existence of that affection. Only time can tell us, therefore, with which of the two diseases we are certainly dealing here.

(5) **Primary Splenomegaly with Anemia.**—This is the last form of the anemias as they occur in childhood with which I have to deal, and I speak of it at all only for the sake of completeness, inasmuch as our patient can hardly belong to any of the subdivisions. von Jaksch's disease should with propriety be put in this class, but its importance and its striking characteristics have caused me to consider it separately. There are only three conditions of which we need to speak.

(*a*) *Banti's Disease.*—This affection is one of young adult life or later childhood. It is not often, indeed, seen during the latter period, but I have come across it occasionally. In this affection the enlargement of the spleen appears to be the most important thing, and the anemia is, at least at first, a minor matter. The splenic hypertrophy is the first symptom appearing, at that time the child being in other respects apparently well. Then the liver becomes involved in the form of a hypertrophic cirrhosis, with jaundice and ascites, and finally there is a shrinkage of the liver. During this period the patient becomes distinctly anemic. There is, it is true, some variation in the order of appearance of these symptoms, and I have seen jaundice develop before much anemia and before any positive affection of the liver could be made out by physical examination. Our patient can be ruled out of this category completely.

(*b*) The next is *Gaucher's disease*, which is distinctly a disorder of childhood. It is often familial in its nature. It appears to begin in infancy or early childhood, but is, in reality, congenital in origin. The chief symptom is a very great and progressive enlargement of the spleen, which often reaches an enormous size. The liver enlarges also, but not to the same ex-

tent. As the disease advances an anemia of the chlorotic type develops, but is never very marked. A diminution in the number of white cells is a very characteristic symptom. The superficial lymphatic glands are often slightly enlarged.

I need hardly discuss this disorder further, so far as diagnosis is concerned. Our boy has some enlargement of the lymphatic glands, and he has a large spleen and some increase in the size of the liver; but he has a leukocytosis instead of a leukopenia, and his anemia is much worse than we would expect to find it in Gaucher's disease.

(*c*) *Hemolytic Icterus.*—This form may bere ferred to merely for the sake of completeness of discussion, because some of the forms exhibit the presence of enlargement of the spleen with anemia. There are two types seen in childhood to be mentioned here. In the one, the acquired or the Hayem type, the disease may come on at any age. There is decided anemia and decided enlargement of the spleen and liver. There is, however, an increased fragility of the red blood-cells, which is a very characteristic symptom, and there is a chronic acholuric icterus. The other form, the familial or Minkowski type, appears oftenest congenitally. There is a diminution in the number of the red blood-corpuscles, and an enlargement of the spleen; and there is also an acholuric jaundice and increased fragility of the red blood-cells. By these two symptoms, if by no other way, we can see that our little patient cannot for a moment be considered as an instance of this disorder.

## TREATMENT OF THE DIFFERENT FORMS OF ANEMIA

It is convenient to consider all the anemias here as a whole, although there is some modification of treatment necessary according to the form. In secondary cases our first duty, of course, is to find the cause and to remove it when this can be done. Next to this the hygiene and the diet must receive careful consideration, and be modified if anything wrong is discovered about them. We must guard against too much confinement to school or to the house in general. The appetite should be stimulated if the digestion

is poor, and we must make certain that the child is eating sufficiently. Life should be in the open air as much as possible. Massage is excellent for the patients who are too ill or too unwilling to take sufficient exercise.

Next of importance is the employment of remedies intended directly to improve the condition of the blood. The first in this class is iron, and after that, or with it, arsenic. To children may very readily be given mass. ferricarb., pil. ferricarb., or ferrum reductum; and to infants and small children saccharated iron or solutions of the pyrophosphate, citrate, or lactate. There are a good many proprietary iron preparations on the market which are undoubtedly useful; but I have never been able to convince myself that they are superior to some of the older official iron formulæ. In many cases a very useful combination is that of the pyrophosphate of iron with emulsion of cod-liver oil. In severe cases, such as the one I referred to in discussing secondary anemia, with a hemoglobin of 15 per cent., very excellent results may be obtained at times by hypodermic injections of a combination of iron and arsenic, such as is used frequently in adult life. I have had fairly good results with this in the anemias of cardiac disease.

In chlorotic cases iron has long been considered a specific, and I believe it is the best remedy we can employ if given in sufficiently large dose. Of course the diet and the hygiene must be looked after carefully, and change of air is very beneficial.

The treatment of pernicious anemia is to a large extent discouraging. As far as internal medication goes, arsenic is probably the best drug, given in gradually increasing doses. In this condition the question of removal of the spleen arises. A number of cases are on record showing at least temporary recovery following the operation. We do not know that it absolutely cures, but it certainly often relieves and prolongs life. For aplastic anemia we can do nothing, but pseudoleukemic anemia we ought to be able to help. Since we do not with certainty know what the cause may be, we should at least hunt for errors in diet and hygiene, and the like, as in secondary anemia, and attempt to correct them. If the patient should prove to be

syphilitic, of course treatment for this disorder should be administered. Iron with cod-liver oil or hypodermic injections of iron and arsenic may well be used. In the case of this little boy I would suggest the hypodermic injection of $\frac{1}{2}$ grain of the green citrate of iron, with $\frac{1}{8}$ grain of cacodylate of soda, and $\frac{3}{4}$ grain of glycerophosphate of soda, given every one or two days. The cacodylate can be increased later if it is well borne. Sometimes these injections cause a local disturbance or a febrile reaction, and in that event the treatment must be stopped for a few days. The question naturally arises regarding the advisability of removal of the spleen in this case. Its consideration is, in my opinion, entirely out of the question. The child is clearly not an instance of pernicious anemia, and the chances of recovery in pseudoleukemic anemia are too great to warrant undertaking such a serious operation. Should the disease turn out to be truly a leukemia, extirpation would also not be advisable. There is one form of treatment for this disease, or, indeed, for any other severe anemia, which I cannot allow to pass unmentioned, *i. e.*, the transfusion of blood. This sometimes seems to start a patient toward improvement, whatever the cause of the anemia may have been. We will have it done here if we fail in other ways. On the ground, too, that the case may be really one of leukemia, we may well try the effects of radiotherapy. In closing I may only mention that in cases of Banti's disease splenectomy should certainly be done early, and also may do good in the Hayem type of hemolytic icterus, whereas it is not to be recommended for the Minkowski type. Little can be expected from it in Gaucher's disease.

**Later.**—The myelocytes steadily increased in the case of the child whose history was reported, reaching even as high as 45 per cent. of the white cells. The Laboratory Department of the University at first based on this fact the diagnosis of leukemia; but afterward altered it, because a steady decrease of the number of myelocytes then occurred until they reached a percentage of 1.5. In the meantime the total number of leukocytes steadily diminished, and the percentage of erythrocytes and of hemoglobin increased. A few *x*-ray treatments

were given, but these were commenced after the great fall in myelocytes and the improvement in other respects took place, and can therefore not be considered the cause. The spleen meanwhile diminished very decidedly in size, and the general health improved in every way. Although still far from well, convalescence is advancing very satisfactorily.

## CLINIC OF DR. FRANCIS X. DERCUM

JEFFERSON HOSPITAL

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# PROBLEMS IN DISEASES OF THE INTERNAL SECRETIONS, WITH ILLUSTRATIVE CASES

I HAVE to show you today several cases presenting most interesting problems in diseases of the internal secretions. Myxedema and acromegaly are already well known to you; the cases which I will show you today deal with other questions equally important, and some of them quite recondite in their nature.

The first is that of a working man, J. S., aged thirty, a Greek; unmarried; admitted to the men's medical ward on October 22d of this year. He complained especially of loss of strength and of vague pain in the abdomen. An examination suggested the provisional diagnosis of an acute cholecystitis.

The family history is negative. There is no evidence of tuberculosis, malignancy, or nervous disease in his family. There are no deformed brothers or sisters.

As regards his personal history we learned that his general health has always been good. He has had no diseases of moment in childhood save malaria when ten years of age. He has never had any venereal infection. His face has always been smooth and he has never been obliged to shave. In 1918 he suffered from influenza and was ill one month.

The illness from which he suffered at the time of his admission to the hospital had existed for some two weeks. He had had some indefinite pain in the abdomen, had been jaundiced, and had noticed that his feces were white in color. There had been some headache, but no vomiting.

Beyond some tenderness on deep pressure on the right side of the abdomen in the neighborhood of the ninth rib, the general visceral examination revealed nothing of importance. In the

course of the examination it was noted that his skin everywhere was very smooth, that there was almost no hair in the axillæ or upon the pubis, and that genitals were very small. Because of these features, the jaundice having subsided, he was transferred to the men's nervous ward on November 27, 1920.

Here the following features, which I now exhibit to you, were observed: As he stands stripped before you, you will note at once the general feminine contour of the body. The breasts are well developed, suggesting those of a young woman, the arms and shoulders are well rounded, and there is a very evident enlargement of the buttocks and of the thighs. The latter are clearly feminine in type. His posture as he stands is graceful. The penis is that of a child, while the testicles are little larger than peas. You note the scanty hair in the axillæ and on the pubis. There is an entire absence of hair upon the face; the cheeks and lips are as smooth as those of a woman; everywhere upon the limbs and body the skin is equally smooth; there is an absence of the hirsute growth so characteristic of the male. When our patient speaks in answer to our questions, you will note that his voice is soft and rather high in pitch. In manner and in gesture he is graceful, his walk is distinctly feminine; in the ward he is very bidable, gentle, and unobtrusive.

Evidently we have before us a male in whom there has been a failure of development of the sex glands together with a failure of the development of those features which Darwin has termed the secondary sexual characters, namely, the beard, the male contour of body, voice, manner, bearing, etc. The peculiarities which our patient presents suggest those of the eunuch of Mohammedan and other eastern countries and of the skoptzi of Russia. In the individual castrated in infancy not only are the secondary sexual characters wanting, but certain other peculiarities are found even more pronounced than in our patient; in whom the testicles, though infantile and undeveloped, are at least present. In the eunuch we have illustrated very forcibly the imbalance of secretion that follows the removal of so important an endocrin structure as the sex gland. The testis, I may remind you, furnishes two secretions—one, from the epithelial tissue, to

be thrown off, and another, from the interstitial tissue, to be retained and which enters the general circulation. This hormone, as such internal secretions are termed, is in relation with the hormones of other endocrine structures. Such a relation becomes especially manifest as regards the pituitary gland, the function of which is profoundly influenced, and, as a rule, in one of two ways. The eunuch, as a result of the unopposed action of the anterior lobe, may, and frequently does, become very tall, grows excessively in height; or he may be somewhat shorter, due to a lessening of function of the anterior lobe, but instead accumulates a large amount of fat the result of the disturbed carbohydrate function of the pituitary. This fat is distributed over the buttocks and thighs, involves the breasts, and is feminine in type. Other less obvious endocrin disturbances are doubtless also present, though less obvious. In our patient, in addition to the absence of the secondary sexual characters, there is clearly an accumulation of fatty tissue over the buttocks, thighs, and breasts, so as to give to the individual a distinctly feminine contour. This secondary endocrin disturbance is, however, less pronounced than in the true eunuch. The proper term to be applied to our patient is not "eunuch," but he is to be classified as a *eunuchoid*, and the condition should be spoken of as "eunuchoidism." It may also be spoken of as "hypogenitalism." It is basic and morphologic, and is, of course, beyond the range of therapeutics. The employment of sex gland grafts can hardly be countenanced on philosophic grounds and, at most, would be wholly experimental.

The second patient I have to show you is equally interesting. It is a boy, A. H., not yet eleven years of age. You will note at once that he is enormously obese, although in stature and length of limb he does not differ markedly from the average child of his age.

The family history contains no factors of moment. Both parents are living and well. A brother, several years older, is perfectly normal. An uncle died of tuberculosis, but there is no other history of tuberculosis or of any malignancy in the family.

The personal history is as follows: The birth was instrumental

and there was some difficulty in having the child breathe properly. Otherwise as an infant he was perfectly normal. In childhood he had whooping-cough, chicken-pox, and mumps. Never had any affection of the heart or lungs; the intestinal tract, too, has been normal; the father adds that the boy has "always had a good appetite" and eats as much as himself. There is no history of accidents or of operations.

The child continued to be normal up to seven years of age. The father has brought with him a photograph showing the child at two years, and another, showing him at five years. Each picture is that of a child apparently entirely normal.

At seven years of age, after he had begun going to school, his parents noticed that he was getting stout. This gradually became more pronounced. By May, 1919, he weighed 150 pounds; by May, 1920, 163 pounds; at present he weighs 180 pounds. The father states that the boy has made unusual progress at school; though only starting at seven years, he is already in the fifth grade, and that he is younger than the other boys in his class; further, that he is unusually strong physically for his age. In reply to questions we are informed that the boy has no headaches, does not vomit, and does not sleep excessively. The reason for my asking these questions will soon become apparent.

As the boy stands before you stripped, you will note that the fatty tissue is distributed diffusely over the back, over the chest, over the abdomen, over the shoulders and arms, and over the legs. The accumulation of fat over the abdomen is especially marked, so that the child stands with head and trunk very erect; indeed, thrown somewhat backward, in order to counterbalance the great weight of the abdomen. It is further noted that, in contrast with the preceding case, the deposit of fat is not feminine in type. There is no special deposit of fat over the buttocks or over the thighs, and while the front of the chest bears a large deposit of fat, there is no special enlargement of the breasts.

In looking at the child we observe that the genitals are of adult size and appearance. There is also an abundant growth of pubic hair corresponding in character and distribution to that

seen in the adult male. Further, there is an unusual growth of hair upon the chest and upper lip, the condition is similar to that seen in youths nearing maturity. Upon the back, arms, and legs there is a decided growth of hair very much like that seen in many adult males; upon the back it is quite pronounced. Indeed, the child is quite hirsute.

In keeping with the father's statement we find the muscular strength to be quite above the normal. His grip is practically that of an adult man. When he speaks in reply to our questions we note that his voice, too, has lost the quality of childhood. The pitch and intonation are almost adult in character. In manner you will observe that the child is not shy or timid, as is the average child; on the contrary, he is confident, self-possessed, assertive, and aggressive. His answers are clear, well worded, and direct. At school, let us repeat, he was in advance of other children of his age; he was mentally active and vigorous; his school reports on his studies have been unusually good.

The general neurologic examination reveals nothing worthy of note. Gait, station, and reflexes normal; no sensory losses. Eyes and other special sense organs normal. General visceral examination negative, save that the thyroid gland is possibly enlarged; the right lobe is palpable. The fatty deposit is diffuse and reveals no embedded lipomata.

The urine is normal; a glucose test revealed some diminution of sugar tolerance. The blood-sugar was somewhat above normal, namely, .191 per cent.

The blood count, however, revealed an unexpectedly high leukocyte count: erythrocytes, 5,050,000; leukocytes, 16,000. Pulse, respiration, and temperature normal.

An *x*-ray of the skull revealed an unusually small pituitary fossa. An *x*-ray of the abdomen resulted negatively; this was also true of a skiagraph of the thorax.

The analysis of this case proves, as you will agree with me, most interesting. To begin with, the case is readily distinguishable from Fröhlich's disease, dystrophia adioposogenitalis. All evidence of intracranial neoplasm, tumor of the hypophysis, as revealed by headache, vomiting, hemianopsic disturbances of

the visual fields or optic atrophy, is wanting. The skiagraph, too, absolutely negatives such a finding, for the sella turcica is unusually small. Finally, the genitals, small and undeveloped in Fröhlich's disease, are in this patient prematurely developed and adult in appearance.

When we turn our attention to the hirsutism present our thoughts turn to the cortex of the suprarenal capsule. A hint is given us by observations made in women. Cases have been observed, for instance, in which women previously apparently well have begun to suffer from menstrual disturbances, irregularities, diminution, cessation. At the same time a marked increase in weight makes its appearance. The muscular strength, too, becomes strangely increased, so that the woman becomes capable of unusually severe or strenuous muscular exertion. Such a patient may believe that she is in greatly improved health. Quite frequently this change is accompanied by abnormal sexual excitability. At times also the patient undergoes a marked change in her disposition. She becomes aggressive, self-assertive, mannish in her attitude. Sooner or later an abnormal growth of hair, a hirsutism, makes its appearance. This is masculine in character and distribution. A mustache-like growth of hair appears on the upper lip; later hair upon the cheeks and chin. At the same time the hair upon the pubis assumes the male configuration; a pyramidal growth upward toward the umbilicus makes its appearance, and at times even a growth upon the upper abdomen and upon the chest. Back and shoulders and the extremities may also present an unusual and even coarse growth of hair. The genitals usually remain normal, though at times an enlargement of the clitoris takes place. Later on the picture changes: loss of weight, emaciation, asthenia, and finally death from exhaustion ensue. Autopsies reveal the existence of tumors which, in all probability, had their origin in the adrenal cortex, and later involve the adrenal medulla and neighboring structures as well. Similarly, autopsies in children such as the one before us have revealed tumors of the adrenals which again involved primarily the adrenal cortex. There is a close relation between the sex glands and the adrenal

cortex; both structures rise in the same blast in the embryo. In the case before us we have every reason to infer that there is present a hyperplasia of the adrenal cortex, and that the precocious sexual development is the direct result of this hyperplasia. How can we account for the excessive obesity? Precocious sexual development dependent upon hyperplasia of the adrenal cortex occurs, it would appear, in two forms. First, there is one in which there is merely the precocious sexual development and the excessive muscular strength. These children are occasionally exhibited in dime museums because of their often extraordinary strength. French authors have applied to them the term "enfants herculés." There is a second form in which, in addition to the two facts of precocious sexual development and excessive muscular strength, there is present obesity. Our patient clearly belongs to this second group. We have reason to infer that the obesity in our case is due to a hypopituitarism. In keeping with this we find the pituitary, judging from appearance of the sella turcica, unusually small. Further, there appears to be an antagonism of function between the adrenal cortex and the pituitary; perhaps in the present instance the hormone of the adrenal cortex overbalances, so to speak, the hormone of an already weak anterior pituitary lobe.

What is the future of such cases as the boy before us? We will dismiss him first, because the story I have to tell you is that of an unfavorable outcome. In due course, emaciation and great weakness replace the obesity and excessive muscular strength, and the children die with all of the symptoms of Addison's disease. It would appear that the neoplasm beginning in the adrenal cortex sooner or later involves the medulla, the chromaffin system, as well, with death as the outcome. Glandular therapeutics appears in these cases to be of no avail; nor are the patients suitable cases for surgical exploration or treatment. You will remember, also, that the skiagraph of the abdomen gave us no information in the present instance; a result which, indeed, I anticipated.

The thyroid gland, I will recall to your minds, is apparently a little enlarged; in spite of the obesity the right lobe is palpable.

I am inclined to regard this symptom as an effort at compensation, *i. e.*, an effort to compensate for the deficient pituitary activity.

In studying cases of precocious sexual development we should bear in mind the rôle played by the pineal gland. It is now a well-known and admitted fact that premature involution of the pineal gland—*i. e.*, hypopinealism—is attended by a precocious sexual development most striking in appearance. The genitals become adult in character in both boys and girls; sometimes the change takes place at a remarkably early age, *e. g.*, at five years or earlier. At the same time the child becomes precocious intellectually; often to a very marked degree. There is, however, no increase in muscular strength and there is no adiposity. Finally, the fact that the lesion in the pineal gland constitutes a tumor formation enables us at once to distinguish such a case from the one before us. There is headache, vomiting, optic neuritis; and moreover—and this is most important—because of the pressure which the pineal tumor may exert on the fourth pair of nerves at their exit from the midbrain, there is apt to be a double superior oblique palsy; other ocular palsies may, of course, also be met with. The case of the boy which we have just studied is clearly not one of pineal disease.

The third patient I have to show you also presents problems of the internal secretions. The patient, a woman aged thirty-five, was admitted to the women's nervous ward on September 24, 1920. She complained especially of pain in the head, neck, and shoulders. The family history was practically negative; both parents and two brothers living and well; one brother dead of an accident. No history of cardiorenal or vascular disease in the family, no history of tuberculosis or malignancy.

Her personal history is unimportant as regards the infectious diseases of childhood. She had measles, mumps, chicken-pox, and diphtheria. Menstruation began rather early, namely, at eleven; it has been at times irregular and regular; always painful, lasting seven days. I am inclined to regard this menstrual history as very significant. She often had attacks of sore throat; tonsillectomy was performed in 1908. In 1909 fell and broke "left

wrist and fingers" and hurt her spine. Was unconscious for a short while. A doctor was called the next morning and her wrist put in a splint. She suffered fainting attacks and dizzy spells for twelve months after this. Then she was taken to the Cooper Hospital. She says she was unconscious for five days. Says "they called it 'spinal meningitis.'" Neck, spine, and legs were rigid. She was in the hospital for ten days; went home for four days, and then returned to the hospital for fifteen more days. Patient says she "was in a semiconscious condition for six days." She was taken home and was sick in bed for two years. Then she was better.

She gives the following account of her present illness: Began in 1912, when her left arm would "turn in and up on her." It was painful, and the pain would go up the arm across the back of the neck to the ears. Then she noticed a slight puffiness on the back of the arms, especially the left. It was painful to touch. Then she also noticed that her right hip was swollen and she suffered from cramps in the legs. These are worse at night. She has been this same way off and on for the last eight years.

When admitted to the hospital it was noted that she was obese, weak, and nervous. As I now examine her before you, you will observe that the fatty tissue is not evenly distributed. Extensive diffuse fatty deposits are found over the abdomen, over the thighs, about the knees, over the back of the left forearm, and to a less marked extent over the back and shoulders. There is also a diffuse increase of fatty tissue over the remaining portions of the trunk and limbs; the face, hands, and feet, however, are free. You will note further, as I examine the fatty deposit, that the patient flinches and cries out and protests. In other words, the fatty masses are painful to pressure. From the account which she has given us it is evident that they are also the seat of spontaneous pain.

This patient presents the two characteristic symptoms—fatty deposit and pain—of the affection which I described many years ago and to which I gave the name adiposis dolorosa. Fatty deposits associated with spontaneous pain or pain upon pressure present themselves under three different aspects. Sometimes

they are small, of variable dimensions, distinct from one another, and readily isolated. Under these circumstances they present what Vitaut, a French wrtier, has termed the nodular form of the disease. At other times, as in the present case, they form extensive diffuse masses variously located. To this condition Vitaut has given the name of the localized diffuse form. Finally, the deposit may not be localized, but may be widely diffused, involving more or less the entire body, save the face, hands, or feet. To this condition Vitaut has given the name of the generalized diffuse form. These distinctions are important to bear in mind, as they have, as we will see, a distinct bearing upon the prognosis.

In addition to the fatty swelling and pain these patients also present as a cardinal symptom—asthenia. The patient is very readily exhausted. This weakness is most marked in the generalized diffuse form, less pronounced in the localized diffuse form, and least marked in the nodular form. It is always a striking feature in cases that are at all advanced. Indeed, the patient frequently becomes bed-ridden by reason of this weakness. Rest in bed, too, is often necessitated by the fact that the pain becomes worse upon exertion.

In addition to the fatty deposits, the pain and tenderness, psychic symptoms or symptoms psychic in origin may be present. Great irritability, depression, and sleep disturbances may be met with. Rarely mental disturbances so serious in nature as to necessitate the isolation or the commitment of the patient occur. At other times the symptoms of hysteria are superimposed upon those of the adiposis dolorosa. This has, indeed, occurred in the patient before us.

When we make a general neurologic examination of this patient, we note a segmental anesthesia or, rather, hypesthesia, involving the left forearm, and, in addition to the pain and tenderness associated with the fatty deposits, we find an exceedingly small area of hyperesthesia—so small that it can be covered by the finger-tip—immediately below the right mastoid process. When this area is touched the patient protests and the head is pulled from side to side in a series of jerky movements. These simulate a convulsion; they are not attended by any modification of

consciousness, and rapidly subside. They almost suggest in their character volitional movements. It is evident that there is in the neighborhood of the mastoid a "hysterogenic zone." Other and more diffuse areas of hyperesthesia are found on the palmar surface of the left hand.

It is quite evident that in this patient the hysteria must be clearly and sharply differentiated from the underlying adiposis dolorosa. The hysteric symptoms may have had their origin in the suggestion offered by some trauma, especially in a patient whose tissues are already painful from adiposis dolorosa.

What most concerns us is the pathology of the latter affection. Autopsies have revealed disease of both the thyroid and pituitary glands. Time will not permit of a detailed account of the findings; suffice it to say that they are of such a nature as to justify the inference that the endocrin functions of both glands are seriously disturbed—possibly a dysthyroidism and a dyspituitarism. In the thyroid gland, for instance, the changes observed may be indicative in part of hypertrophy and in part of atrophy. The changes in the pituitary have been variously described as glioma, adenocarcinoma, and alveolar carcinoma. Certainly enough has been found to indicate a disturbance of pituitary function, and probably a disturbance related to the adiposis present. It is hardly necesssary to allude again to the carbohydrate function of the anterior lobe of the pituitary nor to recall how its destruction is attended by diminution and loss of carbohydrate tolerance and assimilation, and the consequent heaping up of fatty tissue. As regards the thyroid involvement, it is not impossible that this is secondary to the pituitary disease, and is an incomplete effort at compensation.

As far as the pain is concerned, microscopic examination of the fatty masses obtained at autopsy or excised during life, reveal an interstitial neuritis of the nerve-fibers contained in the deposits, and the pain is thus readily explained. As to the cause of the neuritis, however, a speculative answer alone can be given. Perhaps it is due to some toxic or perverted hormone the result of the abnormal pituitary or thyroid action, or possibly to a hormone derived from the fatty tissue itself. How far the latter may

depart from the normal has been shown by the finding within it of numerous hemolymph glands.

What shall we say as to prognosis? Experience shows that cases presenting the nodular form may persist for many years without deterioration of the general health. In the localized diffuse form the prognosis is far more serious; quite frequently in my experience this form passes into the generalized diffuse form in the course of time, and the prognosis of the diffuse form when once established is usually quite grave. After a number of years, frequently only two or three, the asthenia and exhaustion of the patient become so profound that death ensues; or some visceral complication, in itself slight perhaps, hastens, in the already weakened patient, the fatal end.

The question that concerns us as of practical importance to the patient is, of course, that of treatment. Naturally, the administration of thyroid extract suggests itself. This, in my hands, has in the nodular form and in the localized diffuse form, when not too far advanced, yielded at times most satisfactory results, the increase of the fatty deposits being inhibited and even occasionally diminished. In the generalized diffuse form thyroid extract has made, in my experience, much less impression; at times none at all.

The pain can to a great extent be controlled or alleviated by aspirin, salophen, or other salicylates. The asthenia, cardiac weakness, and other symptoms may be met by the administration from time to time of digitalis, strychnin, or pituitrin. Iron may also be given, but the administration of these remedies does not seem to exert much influence on the progress of the case. Perhaps the pituitrin should be given a more extended trial. In the present case, which I have now dismissed from the room, we are apparently losing ground. She has lost instead of gained in strength. Unfortunately, too, she has recently suffered from an intercurrent tonsillitis which has accentuated her weakness.

CLINIC OF DR. B. B. VINCENT LYON

ASSISTED BY DRS.

HENRY J. BARTLE, RICHARD T. ELLISON,

AND

RUSSELL RICHARDSON

JEFFERSON HOSPITAL

## DISCUSSION OF THE TREATMENT OF A CASE OF CHRONIC ARTHRITIS, WITH LAMBLIASIS, BY DUODENAL BILIARY DRAINAGE

THE gentleman whose very interesting case I wish to present to you is a doctor of philosophy, fifty-nine years of age. He has been suffering from arthritis deformans, which began quite insidiously less than four years ago. It commenced with a sense of soreness in both knees when walking and a sense of stiffness in them when sitting. With unusual rapidity it progressed to ankles and small joints of the feet, and almost simultaneously to shoulders, elbows, and more particularly to the wrists and small joints of the hands. There was progressive limitation of motion and a constant sense of soreness and stiffness in the joints that fluctuated in its intensity, but never amounted to acute pain.

He was first seen by me on October 15, 1920, at which time he was considerably better than in 1918, when he took the bath treatments at Mt. Clemens. This failed, however, to arrest the progress of his arthritis, and during 1919 and 1920 Dr. J. Torrance Rugh had given him courses of injections of a stock polybacterin and the oral administration of the Bacillus bulgaricus, which both Dr. Rugh and the patient believed was followed by

some improvement in his condition. But during the summer of 1920 Dr. Rugh inclined to the opinion that the patient's gall-bladder might be the focus of major infection in his case, and referred him to me to determine this fact by direct examination, and to see what might be the effect on his arthritis as a result of a non-surgical course of biliary drainage.

Therefore, on October 15, 1920, Dr. T. presented himself for his preliminary studies. Historically there were obtained from the patient the following facts: His chief presenting complaint was soreness and stiffness and limitation of movement of many joints, chiefly of the hands, wrists, knees, ankles, and feet, although the elbows, shoulders, and vertebral column were also complained of. For three years the doctor had been unable to dress or undress himself unassisted on account of the limitation of movement in hands, wrists, elbows, and shoulders, and for the same period walking had been most difficult even with the help of a cane. There were periods of fluctuating swelling and non-inflammatory edema of the hands, knees, and feet, but no real pain, surface redness, or superficial heat.

As a minor complaint, apparently of little importance to him, it appeared that he had had a chronic cough with muco-purulent expectoration as far back as he could remember.

There was no history of infections except a pneumonia twenty-five years previously and an attack of jaundice six years ago that had lasted for only one week.

Other than this he complained of practically nothing except that he became fatigued unusually easily. It was found, however, that he had had rather progressive loss of weight of approximately 30 pounds during the past three or four years. Historically there were no complaints in regard to the gastro-intestinal system. All foods seemed to agree with him perfectly. There was no nausea, regurgitations, or heartburn; no vomiting and absolutely no abdominal distress. His bowel movements were quite normal as a general rule, occasionally inclined to be slightly constipated, but at no time within his memory has he had diarrhea. This last point in his history is worth while remembering.

On physical examination he appeared quite obviously crippled, walking with a cane with difficulty. His skin was both sallow and suggested an anemia. His conjunctival and buccal membranes were quite definitely pale. His superficial arteries showed a moderate sclerosis. His tongue was clean, the tonsils, teeth, gums, and sinuses were apparently healthy for a man of his years and gave no evidence of having been previously infected. His pupillary, superficial, and deep reflexes were normal. There was no glandular adenopathy. The thorax was somewhat barrel shaped, and his lungs were definitely emphysematous. Scattered throughout both anterior and posterior chests were heard fine crepitant râles with larger moist râles over the larger bronchiæ, which suggested a chronic intracapillary bronchitis as well as involvement of the bronchial trunks. His heart was definitely but moderately hypertrophied, with a somewhat weakened myocardium, but intact valves. The systolic blood-pressure was 125, the diastolic 80.

Abdominally, except for slight tenderness on deep pressure over McBurney's point and over the gall-bladder region, nothing abnormal was found. The stomach and colon were normal in size, shape and position, and were apparently free of adhesions. There was no unusual intestinal peristalsis, borborygmus, or unusual accumulation of intestinal gas.

The examination of his extremities and joints showed a considerable periarticular swelling and thickening in the fingers, wrists, elbows, and shoulders, with limitation of motion and loss of power. In these joints there was crepitation on movement, but no pain unless the joints were overextended. The hands at rest fell into the position of ulnar deflection. The knees and ankles showed a moderate amount of swelling with crepitation, but not as marked limitation of motion as was seen in the other joints. There was no sense of heat or sign of redness in any joints.

Coming now to a consideration of the various technical examinations made in his case, we find that his blood showed a moderate grade of secondary anemia, with a hemoglobin of 65 per cent. (Dare) and a color index of approximately 0.7. His leukocytes were 8220 and the differential count was as follows:

Pmn., 74 per cent; lymph., 21 per cent.; l. monos., 4 per cent.; trans., 1 per cent. There were no eosinophils or basophils. The red blood-cells showed some variation in size and staining reaction, but in general gave the appearance of a secondary anemia. There were no nucleated reds.

Examinations of his urine were, in general, light amber, acid, specific gravity from 1.010 to 1.020, very occasional traces of albumin, no sugar, and microscopically showed quite a number of cylindroids, occasional epithelial cells, but no casts. His phenolsulphonephthalein functional test gave 50 per cent. elimination in two hours.

Analyzing his case thus far, we have no difficulty in recognizing an arthritis, which, according to Barker's[1] classification, seems best to fit into the picture of either a chronic arthropathy secondary to some infectious process, or a primary chronic (progressive) polyarthritis of subvariety (A): pulmonary emphysema with chronic bronchitis; chronic myocarditis; a possibility of chronic intersitial nephritis of low grade, and a secondary anemia. But such an analysis, like so many others, stops short of giving us the kind of information which we most desire, namely, the factors which produced this clinical picture and the factors which might serve to aggravate it. In all such problems it is important to examine all bodily functions and to work out if possible a definite bacteriologic, metabolic, or chemical causation.

Proceeding, then, to a clinical and laboratory study of his gastro-intestinal tract, it was found that his stomach analysis showed a chronic catarrhal subacid gastritis with an inflamed and possibly erosive mucous membrane (Fig. 124). There was no tendency to digestive biliary regurgitation, but on several occasions there was well-marked regurgitation of bile in the fasting residuum, and the mucous secretion was unusually pronounced and very thick and tenacious. The microscopy of the fasting residuum when *unbile-stained* showed a moderate amount of exfoliated gastric epithelium, but a very much larger proportion of extragastric epithelium, swallowed and chiefly identified as coming from the respiratory tract. On the other hand, the

microscopy of the fasting residuum when *bile-stained* showed a very large amount of bile-stained pus-cells with bile-stained cuboidal and short columnar epithelium, simply swarming with bacteria in which a motile bacillus predominated. This very definitely furnished a clue to the possibility of a duodenal or biliary tract inflammation or infection.

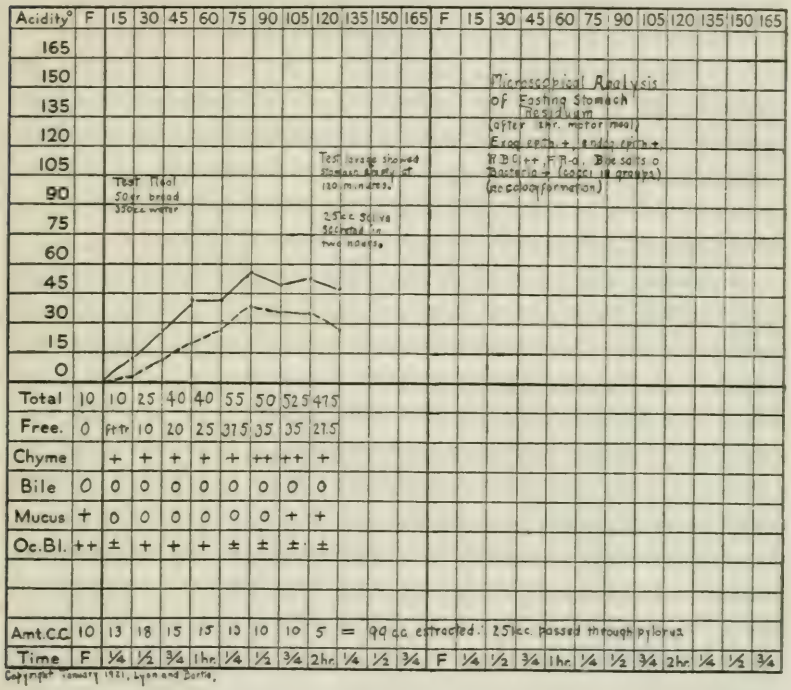
Acidity° F 15 30 45 60 75 90 105 120 135 150 165 F 15 30 45 60 75 90 105 120 135 150 165
165
150
135
120
105
90
75
60
45
30
15
0
Test Meal 50gr bread 350cc water
Test lavage showed stomach empty at 120 minutes.
25cc Saliva secreted in two minutes
Microscopical Analysis of Fasting Stomach Residuum (after 3hr. motor meal) Exog. epith. +, undig. cells +, WBC ++, F.F.-d. Bile salts 0 Bacteria + (cocci in groups) (no coloniformation)
Total 10 10 25 40 40 55 50 52.5 47.5
Free. 0 trtr 10 20 25 37.5 35 35 27.5
Chyme + + + + + ++ ++ +
Bile 0 0 0 0 0 0 0 0 0
Mucus + 0 0 0 0 0 0 + +
Oc.Bl. ++ ± + + + ± ± ± ±
Amt.C.C. 10 13 18 15 15 13 10 10 5 = 99 cc. extracted. 2.5 cc. passed through pylorus
Time F ¼ ½ ¾ 1hr. ¼ ½ ¾ 2hr. ¼ ½ ¾ F ¼ ½ ¾ 1hr. ¼ ½ ¾ 2hr. ¼ ½ ¾
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Fig. 124.

The stomach was then thoroughly washed, astringed, and disinfected according to methods which I have already published,[2, 3] in order to prepare the stomach thoroughly, so that when our tube is allowed to pass to the duodenum our microscopic examination of the duodenal residuum is less confused. In this patient's case the tube entered the duodenum normally in twenty minutes, the common bile-duct was found open, which, as I have already stated, seems to suggest a disturbance in biliary physiology. An examination microscopically of this

very thick, tenacious, bile-stained, mucoid fluid showed extraordinarily large amounts of exfoliated, degenerated, cuboidal, duodenal epithelial cells, apparently broken off in large masses which were simply swarming with Lamblia (perhaps better called Giardia) intestinalis. In addition, there was a great amount of mucus appearing in strands, heavily studded with amorphous bile-salts and pus-cells, and here, as well as scattered throughout all fields, was an unusually heavy bacterial flora of motile short bacilli. In addition, there were considerable numbers of heavily bile-stained short columnar epithelium apparently from the bile-ducts. The giardia were in countless numbers, very actively motile, and were *not* bile stained. Here then we encounter a very suggestive factor either in the causation or in the aggravation of this patient's clinical picture.

Following the removal of the duodenal fluid for a cytologic examination, magnesium sulphate in 33 per cent. solution was introduced into the doctor's duodenum and his gall-bladder was emptied and his bile-ducts drained according to methods with which you are now familiar.[2, 3] This patient's gall-bladder was found to be atonic and contained a static, greenish-brown bile in amounts which varied between 50 and 120 c.c. It was somewhat turbid and contained a considerable amount of flocculent sediment, had a very definitely increased viscosity and an increased amount of microscopic mucus, and very large quantities of amorphous bile-salts, but never any crystals. There was some slight tendency to deepening in the color of his liver bile which suggested the beginnings of a biliary cirrhosis. Cultures from his duodenum and from his gall-bladder biles were examined by Dr. Richardson who recovered the Bacillus coli communior in pure culture and occurring in an unusually heavy growth. A vaccine was prepared from this culture.

Stool examinations showed a moderately strong reaction for occult blood and quite large numbers of giardia cysts, but no uncysted forms either motile or otherwise. His stools were, as a rule, well formed, brownish yellow, with a rather sour odor.

His sputa examinations were negative for acid-fast bacilli, but contained a mixed bacterial flora and quite numerous pus-cells.

Now you will see we can advance one step further in a more intelligent review of this patient's case, and it becomes a question of attempting to determine what effect a colon infection of his gall-bladder and duodenum, together with a parasitic infection of lambliasis, may have had in the production of his arthritis and the other features of his clinical picture, and, if not productive of it, how much they may have aggravated it.

In regard to colon infections of the gall-bladder and duodenum, we have come to the opinion that in those cultures made from these sources when we recover very heavy growths of Bacillus coli sufficient to grossly cloud our broth flasks on standing at room temperature for even a few hours, and which produce a very distinct colon odor within this short period, or when they grow very luxuriant cultures on agar within a similar period, we come to the opinion, as I say, that this is a *pathologically increased* colon bacilli flora. For a number of years there was a tendency to consider the duodenum normally quite sterile. Now, I feel sure, this opinion has been modified, for we do find the colon bacillus and other intestinal flora, more commonly resident in the lower ileum and especially in the colon, nevertheless do in certain apparently normal cases reach as high as the duodenum, but rarely in large numbers unless they find some suitable pabulum in that zone on which to flourish. Reviewing our last 88 pathologic gall-bladders and duodenums bacteriologically studied, I find that Dr. Richardson was able to recover the colon bacillus only 11 times or in 15 per cent. of these pathologic cases, whereas he found 50 per cent. of various strains of streptococci, 25 per cent. of various strains of staphylococci, 8 per cent. of Bacillus subtilis, and 1 per cent. each of Bacillus pyocyaneus and Bacillus typhosus. Therefore perhaps we may be permitted to justifiably consider the recovery of a heavy growth of colon from this patient's case as being a pathologic factor which may have contributed directly to the production of his arthritis. It is to be remembered, however, that where we get these enormously heavy growths of colon bacilli we are dealing with an organism which grows rapidly and has a marked tendency to overgrow the other pathogenic organisms mentioned above with the exception

of Bacillus subtilis and Bacillus pyocyaneus. Therefore we cannot entirely exclude the possibility of pathogenic organisms carried to the duodenal-biliary zone by direct contamination from swallowed purulent sputum from this patient's chronically inflamed bronchial tree, especially since we found cocci in our fresh preparations from his fasting stomach.

Now, for a few moments it will be worth while to discuss the question of the lamblia infection in this patient's case. This parasitical infection shows always a great predilection for, if not an exclusive tendency to attack, the duodenum and jejunum. It is a condition that has been until very recently considered a rarity in temperate zones if one may judge from the literature. Until within the last five years there have been extremely few cases put on record, and the largest series, I believe, occurred within the personal observation of Dr. John C. Hemmeter, of Baltimore, who reported about 16 such cases. A smaller series had likewise been reported by Dr. Frank Smithies, of Chicago. It is unquestionable that this infection flourishes to a greater extent in tropical and subtropical countries, but its occurrence in temperate climates has been shown increased beyond our former beliefs as a larger number of men have become interested in the detection of the disease. The recognition of it has come chiefly from the finding of the encysted parasite in the stools, and there has been a very distinct failure to routinely seek for its presence in its actively motile state in the duodenum. Its incidence may become larger if we extend our routine examinations of the duodenum to include a search for it. During the last six months 3 such cases have come within my personal observation, and all were diagnosed in the fresh state by recovering the living parasite from the duodenum. Within recent years it has been proved that the lamblia may infest other mucous surfaces beside the duodenum and jejunum, since Smithies and, I believe, Hemmeter have reported its recovery from the gall-bladder at operation. Their finding in the gall-bladder, therefore, argues very strongly for the possibility of ascending infections of the common duct and gall-bladder by direct extension from the duodenum, since obviously these parasites are not likely to

have been carried to the gall-bladder by way of the blood-stream.

In reviewing the recent literature on the subject it was found that with one exception[4] the diagnosis of lambliasis was based on the discovery of cysts, and at times free forms of this organism, in the stools.

The question of the classification of this flagellate is still an open one. Noc[5] disagrees with Benson's division into special types in man, mouse, and rabbit, based on difference in size of organism and form of "third nucleus." Kofoid *et al*[6] find that the morphology of the organism of trench diarrhea is the same as that found in the meadow mouse—the "Dachshund rat" of the trenches—and agrees with Porter that the species are transferable. Noc also does not believe in the union of two organisms to form a cyst, but believes rather in a longitudinal division within the cyst, not limited to the formation of two organisms. Ledingham and Penfold[7] believe that there is little doubt that cyst formation is preceded by conjugation of two individuals.

The question of the pathogenicity of this organism is also unsettled. Still takes the extreme position that Lamblia intestinalis is "responsible for a chronic and intractable diarrhea, an infection only minor in importance to amebic dysentery." Daniels and Baumpt agree with him that the flagellate is pathogenic. Emerson, Stiles, Rodenwaldt, McNeal, and Neven-Lemaire think that it may prolong a pre-existing condition, whereas Brown, Park and Williams, Barker, Besson, Albut and Rolleston, and other of the older writers state that it is non-pathogenic.

The whole question was revived during the Great War, principally due to the reported findings of this organism in troops invalided home, especially from Gallipoli, with symptoms of dystentery. In 136 consecutive cases of "dysentery" Kennedy and Rosenwarne[8] found 12 cases in which no organism other than the lamblia could be found, although primary amebic dysentery could not be excluded (these cases had had emetin on their way home). Fantham and Porter[9] found 187 cases of pure lambliasis

among 1305 patients, and in both human and animal lambliasis stool, and at postmortem found that erosion and distortion of the intestinal epithelial cells had occurred owing to the direct suctorial action of the flagellate. Logan and Sanford[10] found 66 cases in 6000 patients, mostly from the northern United States, in 4 of whom it was the only organism found that could account for the symptoms. From their studies they conclude that Lamblia intestinalis is probably pathogenic and that there is no definite syndrome. Cade and Hollande[11] report on 10 cases under their care, the chief symptom being diarrhea generally of long duration with intermissions. Lamblia is also found very frequently in association with other intestinal parasites, and Billings[12] warns that "the mere finding of the lamblia does not prove that it is the sole cause." The clinician must, by a careful study, eliminate other diarrheal affections, in which its presence may be a mere coincidence and not of etiologic importance.

It was generally supposed that lambliasis was limited to tropical and subtropical climates, but with more careful examination it is becoming more evident that the distribution of the parasite must include temperate climates as well.

The most striking thing in a review of the literature is the fact that up to 1917 absolutely no successful method of treatment had been suggested. All the usual anthelmintics proved useless and emetin was of no avail. In a personal communication from Dr. Hemmeter, of Baltimore, and in a paper read before the American Gastro-enterological Society in May, 1920, he states that he has treated several cases of lambliasis by "mechanical washing out of the lamblia by progressively entering the upper bowel with the intestinal tube, further and further. As a vehicle I use Ringer's solution, weak solutions of methyl-blue or thymol." He also states that "compounds that liberate formaldehyd, like hippol in alkaline solution, and pass through the enteroportal circulation many times are effectual (most so in my last 3 cases) because this reabsorption and resecretion through the bile is kept up by the normal physiology a long time." All so-called cures must be examined in the light of the work of Porter[13] and Dobell and Low.[14] The former found that the

number of cysts vary from day to day, and that the periodicity in maximum number of cysts was about fourteen days. The latter's study of a healthy man with a pure infection is most instructive. They examined the stool for a hundred consecutive days, finding sixty-two negative days and thirty-eight positive days, with negative sequences of nine, ten, and seven days. They then gave courses of bismuth salicylate, beta-naphthol, methylene-blue, turpentine, and guaiacol carbonate, but could show no run of consecutive negative days as long as during the untreated period, during and after treatment there being fifty consecutive positive days.

It was not until 1917 that Yakimoff *et al*[15] used arsphenamine in treating, experimentally, white mice infected with lamblia. They used it in 1:300 to 1:1000 solution, giving 1 c.c. for 20 grams body weight of mouse, finding that 1:1000 solution seemed to answer—no lamblia being found in the intestines when mice were killed one to three months after infection.

Kofoid *et al*[6] also used arsphenamine in rats, and found that +4 to +8 the human dose prorated to body weight of rat, freed the animal of lamblia, but that single doses, comparable to the human dose, had no effect; but they did not study repeated doses of this amount.

Carr and Chandler[16] report the use of neo-arsphenamine in 1 case, in man, with relapse after one injection, but no relapse for five months after three subsequent injections of that drug. This use of arsphenamine seems to offer the best hope of curing the infection, but it will need more confirmation before it can be fully accepted.

The description of these parasites varies somewhat according to the authorities which one consults. For instance, Cammidge[17] states that they are from 5 to 12 microns broad, whereas Cade and Hollande[18] state that they are from 10 to 13 microns long by 8 to 9 microns wide. While I have made no attempt to accurately measure these parasites in the 3 cases in which I have found them in the living forms, yet they have seemed to average about 12 to 20 microns in length by 8 to 12 microns in breadth. In shape the parasite on its flat surface has been de-

scribed as being pear shaped, but there are certain ones which I have seen which resemble much more the shape of a racquet, being somewhat more oval than pear shaped.

As to its further description, let me quote from Cammidge, who says, "The parasite is pear-shaped, and is from 10 to 21 microns long, and 5 to 12 broad. In its anterior portion is a more or less well-marked depression, which constitutes the peristome, or mouth opening, of the organism. It is provided with eight flagella grouped in pairs. The first pair are situated on the sides of the peristome and are directed backward. The second and third pairs arise at the projection at the inferior end of the peristome, and likewise project backward. The fourth pair issue from the tapering tail-end of the body. In fresh specimens the third and fourth pairs are frequently agglutinated and cannot separately be made out. In specimens killed with perchlorid of mercury they can usually be differentiated. All the flagella are about equal length, and measure from 9 to 14 microns. The protoplasm is hyaline and finely granular. The organism is surrounded by a fine cell membrane, which can be readily seen in fixed specimens. The nucleus is dumb-bell shaped, and lies at the base of the peristome. Vacuoles and solid inclusions are absent, nutrition taking place by osmosis. The parasites live in the duodenum and jejunum, adhering to the epithelial cells with its peristome. When they reach the large intestine they become encysted, and are then seen as round or oval bodies, measuring 10 to 14 by 8 to 10 microns, surrounded by a very distinct membrane, within which lies the folded organism. This is the form usually found in the feces, and unless there is severe diarrhea or the patient is well purged with salines, the motile parasite does not appear. Fresh specimens examined on a warm stage exhibit rapid but irregular movements."

This description is a very excellent one, but represents their examination by oil-immersion lens up to 1500 magnification. This magnification is not a practical one to be used in fresh specimens obtained from the duodenum. They can be readily recognized under low power and the flagellæ can very distinctly be seen under high power with a dry lens. Those of you who have

not seen them will be provided with a distinct microscopic treat. They usually occur in enormous numbers in strands of mucus, and the majority of them are seen in their lateral aspect where they look very much like the profile of the bowl of a spoon with a little projection backward at the base. From certain angles they also resemble in general the shape of a sickle. They are decidedly translucent, and of rather a shiny silvery gray, with a tendency to bluish refractibility. The lamblia do not ever appear to be stained by the bile. In the fresh unstained preparation it is not possible to make out the dumb-bell like nucleus in the peristome nor to demonstrate any granules. The flagellæ move very actively, and the second, third, and fourth pairs can be most distinctly seen. The second and third pairs appear most visible when the parasite is lying on its side. Owing to the sucker-like action of the peristome it is quite easy to see why they can cling closely to the mucosa, perhaps being attached to individual duodenal cells, and, for this reason, why it is so difficult to dislodge them.

In the fresh living state they are quite motile and retain their active movement for hours if kept in a moist state on a warm stage. They move chiefly in a curious gyrating tumbling fashion, and sometimes whirl rapidly like a spinning wheel. They do not move far in any one direction nor very rapidly even when their progress is unimpeded by mucus or other débris.

Now, returning to this patient's case, there are two interesting features concerning his lambliasis. First, the fact that he has never had any tendency to diarrhea, but has rather been more inclined to be constipated when his intestinal functions deviated from normal. This is distinctly out of the ordinary inasmuch as the larger number of such cases at some time or other will show a very conspicuous diarrhea. Second, it is interesting to speculate where this patient acquired his infection, and on inquiry we find that he has been in subtropical zones only twice in his life, once in Trinidad and Venezuela twenty-seven years ago, and again in Trinidad one year later, and that on one of these occasions he had slept in a bed just recently vacated by a man who

had had the "fever." But our patient states that he was not taken sick. Assuming that he contracted this parasitic infection at that time, it must have been present these many years without ever producing any pathologic symptoms.

Now, having determined the presence of this infection, the next question arose as to how he might best be treated, and, as we have seen from a review of the literature detailed above, the condition when treated by mouth, or even locally by the duodenal tube, using a large number of chemical agents, has proved almost entirely unsuccessful in these cases. The use of arsphenamine, very recently introduced into the treatment of lambliasis, has up to the present time seemed to have the most favorable influence in establishing a real cure. This patient, however, showed a disinclination to have arsphenamine used in his case, and remembering the successful outcome of the second of the three cases, which I have personally seen, under a treatment of continual biliary drainage with duodenal and jejunal disinfection, this plan was submitted for the doctor's approval and was accepted. The principle of this plan of treatment is based upon my feeling that each parasite that can be removed from the duodenum and gotten *outside* of the body before passing through the intestinal tract, at once ceases to be a procreative factor in the production of other parasites, and that by thus limiting the number that remain, our direct chemical parasiticides will have less difficulty in destroying the decreased numbers. This has been borne home to me very strongly by the impression one receives in seeing the enormous numbers of these parasites which one can find in the flocculogranular sediments of the centrifuged specimens of duodenal and biliary fluids. In the beginning literally uncountable thousands of them can be recovered by a single drainage. Therefore, if this drainage is made continuous rather than intermittent, it would seem reasonable that we might thus directly remove these parasites from the body faster than those left behind can breed, and by introducing into the duodenum and jejunum parasiticidal disinfectants several times a day, our chance of killing off the total number in a short period may be distinctly better.

Before starting on this plan of continuous drainage, which was begun on November 26th, this patient had had three duodeno-biliary drainages, on October 22d, November 2d, and November 24th. Each drainage was followed by duodenal instillation of 100 c.c. of 1: 5000 solution of silvol, and this, in turn, followed by a 250 c.c. duodenal enema of Ringer's solution containing 0.5 per cent. sodium sulphate. During this month of intermittent treatment he also received three intravenous injections of 30 grains of sodium iodid. By this time he had shown some distinct improvement in this arthritis, and duodenal examinations for lamblia still demonstrated their presence, but their motility, even on the warm stage, was very strikingly reduced, and they appeared as though distinctly stunned, where before they had been so exceedingly motile.

On November 26th his continuous biliary drainage was begun and carried out for fourteen and a half days, with the following nursing directions: "No lunch, and take duodenal tube about 3 P. M. Wash stomach and do biliary drainage in usual way, and follow with duodenal disinfection with 100 c.c. silvol solution (using 10 c.c. of the 1:500 silvol solution to 100 c.c. water), removing what you can, and follow with duodenal irrigation of Ringer's solution, but use the sodium sulphate, $\frac{1}{4}$ to 1 teaspoonful, only every second or third day to get good intestinal fluid evacuation. Keep the tube in place day and night and drain out duodenal-biliary fluid into bottles day and night, and record amounts. Twice each day irrigate duodenum with 100 c.c. silvol solution 1:5000, and recover what you can. Every third day drain gall-bladder in usual way, and record amounts and describe color and gross appearance and method of flow.

Inject vaccine in increasing amounts according to dosage chart.

"*Feed by mouth.* Liquids every two hours with strained cereals, cream, and sugar. Boiled rice, cream, and sugar. Zweibach, *dry*, and well chewed, butter.

"Pil pancrobilin, plain, 1 one hour p. c. t. i. d.

"Pil hexamethylenamin, gr. 5, t. i. d.

"Powdered caroid, gr. 3, in each milk feeding.

"Keep mouth very clean. Zincloform mouth-wash; tooth-paste (Hunsberger).

"Chew gum constantly, and spit out saliva."

This treatment was carried out at the patient's home, and every third day specimens in the original bottles were sent immediately to the office for cytologic examination. On December 1st lamblia were no longer demonstrable in their fresh state, nor were any cysts found in the stools, and there was a very remarkable improvement in the condition of his joints. The swelling was markedly reduced, and there was a very decided increase in the limits of mobility. From December 1st, throughout the balance of his continuous treatment to December 15th, no further lamblia were demonstrated. On December 2d his tube was withdrawn, and full feeding was resumed for three days, when the tube was reintroduced and kept *in situ* in the duodenum until it was finally removed. During this period of continual drainage, which totaled fourteen and a half days, there was extracted from his body and recovered in our collection bottles 248 ounces, or $1\frac{3}{4}$ quarts, of mixed bile and duodenal secretions, or an average of 17 ounces a day. It is quite interesting to note the relative amounts of drainage recovery during the twelve daylight hours from 6 to 6, showing a recovery of 168 ounces of bile as against 80 ounces of bile recovered during the night hours from 6 P. M. to 6 A. M. It was also extremely interesting to watch the improvement in the character of the bile. The viscosity, due to its great mucus increase, gradually thinned out and approached very much more the normal. The gall-bladder bile which in the beginning was a static deep olive-green black, gradually lightened in color to approach much more the normal golden yellow, and similarly the "C" bile, or liver bile, which in the beginning suggested the deepened color of a biliary cirrhosis, gradually cleared up and returned to the normal light lemon yellow.

Coincidently with this there was progressive improvement in the condition of the joints, which had increased their limits of motion to such an extent that on the fifteenth day of his treatment he was able to lace his own shoes.

Now let me tell you one disappointing sequel. On December 26th Dr. T. reported for another course of intermittent duodenal biliary drainage, and at this time Dr. Ellison had no difficulty in again demonstrating the presence of actively motile lamblia from the duodenal biliary fluids. This, you see, is only thirteen days after his period of continuous drainage, during the last ten days of which we were entirely unable to demonstrate living or encysted lamblia. Now, how are we to interpret their reappearance? There was one very obvious possibility, namely, that we had not succeeded in completely destroying the duodenal-jejunal infection by this plan of treatment, although it had been entirely successful in a case so treated last summer, which has remained lamblia free for several months. Another possibility, whose likelihood appeals very strongly to me, is that in this present case the doctor's gall-bladder is actually infested with these parasites, and that these organisms were not chemically attacked by the use of the silver salt introduced into the duodenum, and that the reinfection of the upper intestine may have resulted from the continuous presence of these parasites within the gall-bladder. This can only be guessed at, of course, short of operative removal or operative drainage of his gall-bladder, although we have felt that early in the study of his case we found larger numbers of these parasites from the flocculo-granular precipitate occurring in the gall-bladder bottles. One other possibility was considered, namely, that the lamblia might be carried down from the mouth or respiratory passages and be demonstrable in the sputum. They were diligently sought for in several specimens of the sputum, but were never found.

I feel sure that there might be a very great likelihood of arresting this infection by the use of arsphenamine, particularly if the solutions were introduced directly into the duodenum as well as by rectal instillation, for it is likely that a large part of this drug would be absorbed into the portal circulation and re-excreted through the liver, and thence pass directly to the gall-bladder.

In retrospect I am inclined to feel that the lambliasis in this patient's case did not have any direct pathogenic bearing on the

production of the arthritis, inasmuch as at no time has it been possible to prove, or even to suggest, the likelihood of any abnormal symptomatology resulting from their presence. We cannot be so equally sure, however, that this parasitic infection has not had some bearing on aggravating the arthritis and the rest of the clinical picture.

In the concluding moments of this hour I wish to call your attention to the great possibility that may lie in this method of intermittent or continuous drainage of the duodenal-biliary system, in the treatment of certain constitutional or infectious diseases. I have secured a quite remarkable success in the treatment of several cases of arthritis similar to this one, except that a hemolytic variety of streptococcus was the infective agent in several cases of biliary cirrhosis of long standing, and also in one very remarkable case of hemolytic jaundice with splenomegaly and apparently well-advanced biliary cirrhosis, in whom not only was there secured very marked improvement in a symptomatic sense, but distinct lessening of the jaundice and a subsidence in the enlargement of the spleen, so that it could no longer be abdominally felt, whereas before it had presented into the abdomen as far as the navel. This case is worthy of being reserved for a detailed discussion in a future lecture.

It has seemed to me that in this group of cases where a patient is being chronically poisoned by a retention of bile or liver excretory products, that the mischief is kept up because much of the load that the liver is forced to carry comes back to it again and again by the reabsorption from the portal circulation of the poisonous elements normally excreted in the bile and passed into the duodenum for exit through the intestinal tract. The liver then never has a fair chance of reducing its poison load and of recovering a normal function of its liver cells. Therefore, if by a procedure of frequent intermittent or, perhaps in suitable cases, continuous biliary drainage we remove from the body several pints of this poison-laden bile, and not permit it to pass through the intestinal tract, where a portion of it will be reabsorbed by the portal circulation, we thus give the liver its big chance to recover from its toxema.

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## CLINIC OF DR. E. J. G. BEARDSLEY

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# THE NECESSITY FOR AND THE IMPORTANCE OF ROUTINE PROCEDURES IN CLINICAL MEDICINE

IT is often a thankless task to recite commonplace medical truths. This is particularly likely to be true, no matter how important or vital the lessons that can be learned from them, if the stated facts are well known to the audience or to the individual addressed.

The recital in this historic clinic, however, of long-known, commonly acknowledged, and incontestable facts can do no possible harm and may influence a certain number of my hearers to their advantage and, what is far more important, to the advantage of their future patients.

It is only fair to warn my audience that every statement that will be made in the lecture has been made scores of times before and has been made in this clinic, from time to time, by authorities in medicine since the opening session of our school in medicine. The statements to be made today, however, are just as true, just as practical, and quite as important as they have ever been in the past, and a recognition of the facts just as necessary for true success in the practice of medicine.

The excuse for such a lecture lies in the potential good that may be derived from it. Any statement that will tend to visualize the responsibilities of medical men or any suggestion or plan that will, or may, aid in making physicians more helpful and efficient is of undoubted value. Before discussing the practical importance of routine procedures in clinical medicine, and particularly before directing your attention to the technical

details of such procedures, it will be well for me to remind you of the existence in each of us of at least two unfortunate and troublesome traits. I refer to carelessness and to lack of scientific thoroughness in our professional work. These two traits have in the past, do in the present, and will continue in the future to lead more physicians into the preventable errors of professional life than all other causes combined. These traits, seemingly unimportant, have since the beginning of medical history proved to be the very vulnerable Achilles' heel of the profession. The only safe and sure antidote for these practically universal faults is the adoption of, and the rigid adherence to, a practical system of routine procedures that will safeguard our patients as well as insure our professional lives against the evil effects of these very common and very human failings.

One fact that we must recognize, acknowledge, and resolutely face is that although the trait of carelessness and the common tendency toward lack of thoroughness may prove to be simply an irritating deficiency or weakness in a man or woman whose occupation or business is not vital to the public welfare, the existence of the same traits in a physician, in whose care is entrusted both the health and the very life of his patients, may prove to be a very serious and dangerous defect, not only to the health of the individual patient but also to the public health as well. There is no profession in which it is so essential that carelessness and lack of thoroughness in one's work be reduced to a minimum as in the work of a physician. The tendency to slight certain features of our work is constantly within us and must be guarded against at all times if we are to carry on, as we all wish to do, the best kind of medical work.

Careless or indifferent work in medicine transforms that which should be an ideal profession into a "privileged business," the transactions of which are, in the nature of the case, unfair to the patient, the public, and the medical profession.

We physicians are licensed by the authorities of the State to practice the art of healing the sick and, except for an enlightened public opinion, our own conscience is our only guide as to how thoroughly and well our work should be done.

We live in an age in which the profession of medicine is freely and commonly criticised or, rather, one commonly hears representatives of the profession criticised. The statement is commonly made that physicians, not infrequently, fail to return full value in scientific diagnosis, care, and thought for the money received from patients. The most distressing feature of such criticism is, in certain cases, its justice.

That it is unfair that the entire profession should be condemned because of the failure of certain members to live up to their obligations is obvious, but that there should be so many occasions for just complaint against members of the medical profession is most unfortunate. No lay critic can possibly be as well aware, as is the physician, regarding the amount of inferior medical work done by a certain proportion of the members of the medical profession. It is important, therefore, that the united profession should earnestly seek for the causes of the poor or indifferent professional work and seek to apply such remedies as will lead to a correction of the evil.

Just as the lack of reasonable efficiency in a certain proportion of medical students casts serious reflection upon the educational opportunities and training of a medical college or hospital, so does the lack of proper professional ideals and lack of a standard of reasonable efficiency among graduate physicians reflect discredit upon our ancient and honorable calling.

It is a well-known fact, and a statement of it not likely to be disputed, that there has never been a time in the history of medicine when the scientific preparation and training for those who seek to become members of the medical profession has been so generally satisfactory. Certainly there has never been a time when the clinical and laboratory training for undergraduate medical students has been more thoroughly carried out than it is today. Why then should there be so much perfectly honest and essentially just criticism of the professional work of certain medical men? The answer lies, at least in great part, in the lack of a proper sense of professional responsibility and a lack of proper ideals in a certain percentage of licensed physicians.

Many of these licentiates in medicine are so-called "good

business men" who mistake the relative value of quantity of medical work done for quality of real professional service rendered. If judged by proper professional and scientific standards a great deal of the medical work performed by such physicians would be condemned. A greater number of medical offenders, however, comprise men who gradually and almost inadvertently drift into careless medical habits and methods for the lack of some impelling example to do better and more efficient work.

The hope for better medical ideals and therefore for better medical work lies in the students of today and tomorrow as well as in the teachers and leaders of the profession, and seems to me to largely depend upon whether the latter are willing to take the time and opportunity to inculcate higher and better ideals along with the acknowledged superior technical education and training into the minds and hearts of our coming generations of medical practitioners.

The medical profession of today needs nothing so much as it needs leaders who combine the necessary qualities of the highest ideals with the best modern scientific training.

A medical revival, in which each representative of our profession would search his medical life, instead of his soul, for the sin of inefficiency would probably have a most desirable and stimulating effect upon all of us. Oh, for another beloved modern Hippocrates possessing a personality similar to and being endowed with traits resembling those of the great Osler so lately taken from us and so sadly missed! No medical leader in this or any other country ever exercised a greater influence for good than Sir William Osler. And no physician was ever more greatly admired or more truly loved. He was, in very truth, a Master in Medicine, a leader and a teacher beyond comparison, a noble and true physician, and a great and good man.

One of the happiest and most highly valued privileges of a medical teacher is the favorable opportunity afforded by his position for observing and for keeping himself informed of the success that comes to his former students. As a teacher and consultant his daily work very naturally brings him into intimate relations with the family physician and with the patient

and his family, and frequently this intimacy enables him to fairly judge the quantity and quality of the medical services rendered. The satisfaction that a teacher feels in witnessing or in learning of medical work excellently performed, especially if the work was performed by former students, is indeed great, while the sense of humiliation and keen disappointment experienced when a teacher becomes aware of professional work carelessly, badly, or unethically done, particularly if a former student is responsible, is most disturbing to one's pride in one's school or in one's profession.

Professional success of the highest type in medicine can and should be judged by the amount and kind of professional work performed in the interest of the patient, the public, and the medical profession rather than by the financial income and material prosperity of the physician. Financial success that has its foundation based upon industry, efficiency, and the best kind of professional work is not only admirable, but it is and should be a source of healthy inspiration to all medical students and physicians. An income, however, that is acquired as a result of, consciously or unconsciously, lowering one's personal or professional ideals and, more particularly, when gained at the potential sacrifice of a patient's health, as a possible result of careless or inefficient professional work, is not to be envied by any physician worthy of the name. In the medical profession if one does his work faithfully, skilfully, and scientifically, and tries, as consistently as possible, to practice the precept of the Golden Rule in his relations with his patients and with his fellow practitioners, he will be sure to achieve an enviable and honorable success.

No truly interested teacher can come into daily contact with medical students without becoming greatly interested in their professional futures and without becoming deeply interested and concerned in the practical problems of medical education. The more intimately a teacher is associated with undergraduate students, the more clearly he comes to realize that the chief difficulties that the students encounter in their postgraduate lives are caused by the same lack of routine or system in their

professional work that so frequently handicaps them in their undergraduate studies.

After being connected with a medical college in the capacity of a teacher for a number of years interest in students is bound to extend far beyond the confines of one's own school, since all younger medical men become in one's mind, as younger brothers who are traveling the same, none too easy road, over which one has made progress with difficulty himself. The rough places in this road that leads to a useful and honorable place in the profession of medicine are many, and there will never be too great a number of those who travel the road who will pause to look back and to point out with sympathetic understanding a few of the rough places. What a few words of cheer and encouragement mean to the student, the intern, or to the young practitioner, the majority of whom usually need such encouragement very badly, can never be realized by the minority who need them not, and who, quite possibly, have never felt the need of inspiration or stimulus.

The writer cherishes in his memory, and will while life lasts, the happy recollection of kindly expressions of interest from the lips of those great men in medicine, unfortunately no longer with us except in grateful memory, whose habit it was to cheer young men upon their way with an encouraging smile. If every discouraged student, resident physician, or struggling practitioner of today could be greeted and inspired by that Master Physician, Osler, or by those kindly Knights of Medicine and Surgery Roland G. Curtin, James Tyson, John Musser, E. L. Traudeau, W. L. Rodman, Joseph Hearn, or J. William White how fortunate they would be.

Fortunately for you and for me and for the many students of the future many of the kindly hearts that greeted and encouraged me through smiling, frendly lips are not stilled in death, but their friendly personalities remain like helpful beacon lights whose rays of friendliness, sympathy, understanding, and good will light, and will continue to light, many a discouraged professional brother on his way.

You love the names and you love the men whose kindliness,

as well as their superior professional skill, has engraved their images in my heart. The thought of the tremendous influence for good that has radiated and continues to emanate from these men makes me very thankful that Jefferson Medical College, as well as the medical profession of this famous old city has been and is so richly blessed by their presence and by their work. We, of this famous old school, must keep in mind the fact that the Jefferson Medical College occupies a unique position in the medical world. The fact that it is not a part of a university system prejudices many, while the lack of a sufficient endowment handicaps both trustees and faculty in their endeavor to provide the best course of study in practical medicine that can be obtained. The school's ancient heritage of a genuinely practical curriculum and its near century of honorable and useful past is not sufficient to insure its successful future in these days of almost unreasoning objection to the independent medical school by those that guide the medical destiny of the nation. If our school is to have as honorable and as useful a future as she has had a glorious past it will require that trustees, faculty, and students must be embued with a desire to be connected with the best and most practical school of medicine in the country and each must insure its good qualities by unselfishly devoting earnest thought and hard work in its interests.

The medical school is poor indeed that merely gives to a student his technical training in medical science, no matter how excellent that training may be, if it does not also inspire him by its traditions and through the influence of its faculty with the desire to make his medical life worthy of being an alumnus of his alma mater. A medical school that does not inspire and influence its students to do better professional work than the average patient can afford to remunerate for (in coin of the realm) should be properly classed as a "Business College." We students of medicine, old or young, must not forget that Section I of Chapter I of the Principles of Medical Ethics, which our profession adopted as our official rules of conduct, states that "A profession has for its prime object the service it can render to humanity; reward or financial gain should be a subordinate

consideration. The practice of medicine is a profession. In choosing this profession an individual assumes an obligation to conduct himself in accord with its ideals."

If each student and practitioner of medicine could keep ever before him a full realization of his responsibility as a member of a loved and trusted profession to conscientiously live up to the principle of the Golden Rule in his relations with his patients there would be a great improvement in the science of medicine.

Just as those physicians we meet influence our lives and behavior by their attitude toward their profession, their patients, and toward other practitioners, so, unconsciously, do the writings of those whose words we read. Who has not responded to the inspiration that the beloved Osler wove into the text of his essays? Did ever a student or practitioner read his delightful essays, especially those in the volume whose first essay was entitled "Æquanimitas," who was not a better man and a better physician for having read them?

The profession needs medical geniuses to point out new and better methods of research and investigation; it needs an ever-increasing supply of excellently trained scientitsts and investigators; it needs more and more to have its ranks filled with thoroughly educated and well-trained physicians, surgeons, and specialists, but it also needs leaders of the very highest and best types to inspire us to do our very best work in the every-day practice of medicine.

It is well for us to remember that year in and year out the greater part of the medical work of this or any other country must be performed by the medical practitioner of average gifts of intelligence, education, and training.

If such physicians possess high ideals, are endowed with that none too common virtue, common sense, are fundamentally and scientifically honest, and continue to be never-tiring students of human nature as well as of medicine, they will be sure to be a source of great comfort to their patients, a bulwark of strength in their communities as citizens, and an honor to their profession.

In the every-day work of medical practice, as in the world of business, the qualities of honesty, integrity, and industry are

far more important than brilliance of intellect or flashes of genius, valuable and stimulating as are these latter traits.

It has been said by competent, unbiased observers and critics of modern civilization that medicine is the only profession that intimately and persistently concerns itself with the continued education of its graduates. It is certainly true that among the members of no other profession does there exist such a universal recognition and ready acknowledgment of the practical necessity for continued study and investigation of the daily problems of one's life work as among progressive practitioners of the medical art. The leaders of our profession have many times pointed out that intelligent medical practice exemplifies a never-ceasing postgraduate course in scientific medicine. Even among those physicians who, for a variety of reasons, have neglected the scientific aspects of their medical work, and as a consequence have fallen into evil (medical) ways, there exists, nearly always, a clear recognition and ready admission of their professional deficiencies and a sincere desire to improve the quality of their work.

The question that naturally arises in our minds is, Does the lack of reasonable efficienty in a certain proportion of medical practitioners reflect discredit upon modern medical education, or is the explanation for the fault to be sought for in the unscientific performance of medical duties by careless practitioners? In carefully studying this question it becomes apparant that there still exist deficiencies in our general as well as in our medical educational systems and methods that require the thought and attention of experts for their proper correction.

Every physician is well aware, however, that no matter how excellent his training and scientific education may have been, he must constantly strive to keep informed as to the advances in medical knowledge.

As has been already pointed out, the mobilization and war services of large numbers of the medical men of the country during the past four years has offered an unexcelled opportunity for a critical survey of the practical results of the courses of study in our medical schools. This survey has been based upon an extended study of the professional qualifications, technic, and

efficiency of an unprecedented number of graduates, and offers an exceptional opportunity for detecting weak points in our system of medical education and in the profession. For the first time on such an immense scale there has been held in all the services what, in effect, has proved to be a national, non-sectarian, practical examination. The closely supervised work of each medical man in the services has resulted in the technical strength or weaknesss of a medical officer being revealed to him and to his superiors through the observed and recorded results of the routine of his daily work. It is, perhaps, unfortunate both for the importance and value of the records and for comparison as well as for its educational advantages that those practitioners who served the country so well at home in a civil capacity could not also have profited by the enlightenment and stimulating experience of having their work supervised, occasionally criticised, and sometimes condemned by those in positions of authority. That serious professional deficiencies and even gross incompetence existed in a certain proportion of medical men in the services there can be no doubt, but it is also true that the explanation of the glaring professional deficiencies found should be sought for, first, in the inherent faults of our former system of education, lay as well as medical; second, in the serious existing defects of organization and curricula of many of our present medical schools, and third, but by no means least, in the possession of the army surgeon of the very human failings of carelessness and lack of thorough scientific investigation and study that is encountered, all too frequently, in the daily work of civilian practitioners as well as in the work of physicians who happen to wear a service uniform. One of the lessons that can be learned from our recent military experience is that the proper supervision and control of the professional activities of medical men by some respected central authority is necessary, practical, and wise.

If it was necessary to supervise the professional work of service physicians who were selected after a careful physical and mental examination as to their qualifications for the duty of caring for a specially selected group of citizen soldiers, supposedly

in perfect physical condition, how much more necessary it is that the work of physicians who are to have charge of that great body of unselected citizens, men, women, and children, be supervised and their efficiency be determined.

What a wonderful advance it would be for our profession were it both possible and practicable to have selected a number of the finest types of physicians, clothe them with the authority of some central medical authority such as the American Medical Association or the State Medical Society of Pennsylvania, and have them make a personal canvas of all the physicians of this commonwealth. Such representatives of our societies would be chosen for their practical knowledge of men as well as of medicine, for their tact and diplomacy as well as for their high ideals. Could there be any more beneficial influence upon the members of our profession than to have a respected and admired representative of an authoritative professional body call to talk over in a friendly, helpful way the daily problems of medical work. Would not the effect of such a visit stimulate us to do better work? Would not our office records, our laboratory work, our medical libraries, and our entire attitude toward our profession be healthily stimulated?

If such a plan could be instituted would it not afford many opportunities for aiding those physicians who were in need of help of various kinds, for transmitting old and new practical and helpful information as well as for obtaining a survey of the practical needs of members of the profession?

Is it conceivable that a modern business could be conducted with the same lack of method that certain physicians use in carrying on their daily work? Such inefficiency would mean disaster in the business world if competition was keen and the competitors equipped with better systems. Let me urge the men before me who have not already learned the necessity of adopting a system in their study and work to do so. All successful systems are based upon routine procedures, and the practice of medicine can be made to adapt itself to such a process or method with resulting satisfaction to the patient as well as to the physician.

There are physicians who feel that it is quite beneath our professional dignity to even remotely compare our work with that of a business or trade, but it will be decidedly beneficial to all of us if we will adopt the best ideas of the business world, making such alterations as are needed, to practically apply the important and basic idea of efficiency to our own work.

It is a grave reproach to the medical profession that the high ideals and principles of the best types of business men and business systems are frequently so much higher and more efficient than are the ideals and systems that one not uncommonly encounters in members of our own profession.

In any reputable business of today all goods are guaranteed, and if not satisfactory can be exchanged without cost or prejudice to the purchaser. Standard goods are the rule and not the exception, and sharp practices in business are infrequently met with. Can we honestly believe that all medical services are guaranteed or that the patient always receives the best care and attention that the physician he consults is capable of giving him? If we do not give to each patient that consults us our best services we lower our own professional standard as well as also lowering the standard of the profession in the city or town in which we are licensed to practice. Do you think that a modern business could long remain solvent if careful records of its transactions were not recorded and preserved? What proportion of physicians throughout our land keep proper professional records of their patients, records that are complete enough to be scientifically valuable? To assume the professional care of patients without the use of records is not unlike attempting to tell the time by consulting a clock that has but one indicating hand. No physician's memory is to be depended upon for details regarding a patient seen at some more or less remote period, and a carefully kept brief record of the essential scientific facts is a most valuable aid to any physician. For the average physician an elaborate system of records is neither practical nor wise. It is far better to adopt a simple, easily conducted system of records *that will be used* than to begin with an elaborate and expensive system that will be inefficiently kept and soon abandoned. The essential

matter is to have *a* system of both records and procedures and to continue their use until you replace each for an improved method.

To the undergraduate student such a plan will seem natural and easy, and I hope that you may all be able to resist the temptations that will surely arise to cause you to fail to complete records or to take so-called short cuts in certain cases because the record does not seem, at the time, important. You will be amazed to learn how easy it is to neglect to record the most essential facts relating to a case unless you adopt a strict routine. To neglect to record such essential findings as the weight of the patient, the temperature, the pulse-rate is so easy unless one refuses to yield to the temptation no matter what the excuse may be. If the medical graduate, especially the recent graduate, could early learn the benefit and importance of systematically carrying on his professional routine without regard for what the patient or the patient's friends were thinking, it would be a tremendous asset for him and for scientific medicine. To take an elaborate and complete history of every patient that one sees professionally is an ideal that is impractical for the average practising physician. To attempt to take such an exhaustive history upon one's first visit to the patient or upon the first visit of the patient to you is, as a rule, undiplomatic. The average patient must, in many instances, be gradually educated to appreciate the refinements of medical practice, and he often resents inquiry that, as far as he is capable of judging, has little or no bearing upon the features of his own illness that appear to him to be the most important.

There will be sufficient time and far better opportunity for obtaining the less important details of the history at a future time, particularly as one is frequently compelled to add to the original history notes of essential facts that are reported from time to time during the later acquaintance with the patient or with the patient's family or friends. No experienced physician can doubt the importance of a carefully elicited medical history, and no one will question the statement that the carefully preserved and accessible record of such a history indicates that its possessor is a

better trained and better qualified practitioner than he would be without such signs of efficient supervision of his patients. It is not always the highly technical details of a patient's examination that are of the greatest value in aiding to make a correct diagnosis. To weigh and to record the weight of the patient at each infrequent visit is a simple procedure, but who will deny its helpfulness? The memory as well as the impressions of the patient and of the friends and family are not to be relied upon concerning details in even the immediate past, and, as for the physician, his mind should be fully occupied with far more important matters than attempting to carry in his memory details of an examination or medical history that can easily and far more safely and profitably be properly recorded and filed for reference. To know and to record the patient's temperature, the number of respirations in certain cases, and the heart rate may seem absurdly simple to mention, and yet the diagnosis of many an obscure condition depends much more upon the knowledge to be gained from such seemingly prosaic and unimportant observations than it does upon the physician being deeply learned in highly scientific lore.

Beginning with Hippocrates all the great medical leaders have advocated the prime necessity of cultivating the art of observation if one would become a skilled diagnostician. The importance of inspection can never be overemphasized if the observer has learned or will learn not to be content to rely alone upon what he observes, but will bring into use all the other aids in diagnosis to confirm or refute the impression gained by observation and careful inspection. There are few lessons more important for the searcher after truth in clinical medicine to learn than the necessity for a good light in making a diagnosis, and no less important is the wisdom of having the part examined as free from covering as the circumstances render practical, possible, or wise. True modesty is of the mind and heart, and although the natural feelings of delicacy in a patient should be, as far as practicable, considered, any false ideas of modesty that are encountered should be counteracted by proper education. The nearer we approach the ideal of examining the patient in a well-lighted

room and in a practically nude state, the more quickly will clinical medicine free itself from many common and often ridiculous errors. One must use tact and judgment, it is needless to state, in adopting indiscriminately such a seemingly radical plan of examination and one must provide suitable loose covering so that female patients will not be unnecessarily embarrassed or offended by the examination. The more intelligent the patient and the more efficient the medical profession in the community, the less hesitation there is in carrying out with perfect freedom the necessary examinations.

The essential thought for us is that we must not allow the patient's ignorance, indifference, or actual dislike for an examination to prevent our making such examinations as we know are essential. The patient is frequently indifferent in the matter because he does not realize the importance or the necessity for a thorough examination before a correct diagnosis can be made, while the temptation for the physician is to neglect the examination because of lack of time and because of the patient's mental attitude toward the matter. In one's office and in all well-regulated hospitals it is practical to have a supply of loosely fitting kimonas that are so made as to allow portions of the garment to be easily lifted in order that various areas of the body may be carefully examined without the patients realizing that they are in reality disrobed.

Professor Osler was accustomed to state that there were three requisites for a careful and complete physical examination: "A good eye, a good light, and then more light." Although this aphorism was commonly given to particularly emphasize the necessity of careful inspection in the diagnosis of aortic aneurysm, the same truth is applicable to all diagnosis by inspection.

You will all appreciate that what may appear to be a very obscure malady in a dark and gloomy ward or office will often prove to be an easily recognized condition if the examiner can have the advantage of seeing the patient in a well-lighted room.

Concerning the particular method of any routine examination

it can be stated with truth that it makes little difference as to the order in which the examination is carried out, as long as the examiner uses the same routine order in each patient.

If one adopts the method of general inspection first and then especially inspects the scalp, face, eyes, ears, nose, mouth, teeth, tonsils, throat, cervical region, etc., and continues the examination by inspecting the thorax, epigastrium, abdomen, sexual organs, extremities, and does this in each particular patient, he will soon learn to make such an examination quickly, accurately, and thoroughly. If, on the other hand, a student or practitioner evolves a different order or system of examination and *sticks to it* his plan will be (for him) equally efficacious.

It is often stated, and more commonly than stated, believed, that such an examination as has been outlined is only practical for the specialist whose fees are supposed to be large and who can thus afford to take the time necessary for completing such a thorough examination.

If this statement or belief were true, which it is not, it could only mean that when any patient was ill with a severe, an obscure, or a chronic illness it would be the safest and best, not to mention being the most economical, plan to consult a physician who would take the time to make the necessary examinations that would lead to the discovery of the cause of the symptoms and thus to the rational therapy for the condition. There is one undisputed fact in practical medicine, and that is that proper treatment must, of necessity, depend upon proper diagonsis, and that proper diagnosis can only be made by careful, systematic, professional inquiry. It is well for us to acknowledge that unless we are willing to spend the necessary time in examination and expend the necessary thought upon the diagnosis of our patient's illness that it would be quite as well for the patient and far better for the reputation of our profession if the patient did not consult us, but rather sought some one who would give him the required attention. A patient feels that when he consults a physician that the latter assumes all responsibility in the case, and the patient is justified in thinking this. It is well for us to remember, however, that when the physician assumes the responsibility the

patient's anxieties and fears are lulled to sleep even when unrecognized dangers still menace him.

If we, as professional advisers, overlook and ignore the early symptoms or signs of such diseases as nephritis, diabetes, tuberculosis, and similar disorders through lack of thoroughness or through neglecting essential tests, we must admit that we are culpable.

It is at least a debatable point as to whether the average patient that is not thoroughly examined in a physician's office does not occupy as much of the physician's time as would be necessary to examine him thoroughly. The patient must be seen and conversed with and it takes as little time to examine a patient as it does to explain the nature of the illness by more or less shrewd professional guessing. Many of the doctors who speak of having a "big business" see many patients in a day, but miss all the real professional pleasure of their work by never performing it in a truly professional manner. Such physicians treat obvious symptoms empirically without making any serious attempt to discover the exact cause of the symptoms. That many of these men are extremely clever in recognizing various physiologic and pathologic states as well as clever in treatment makes it all the more regretable that they do not devote their undoubted skill and talents to a more serious study of their patients.

Any criticism of such superficial methods is usually met with the excuse that the fee collected is too small to compensate for a thorough examination. One must bear in mind, however, that such reasoning is dangerous and utterly fallacious. The patient that makes five visits and pays five small fees is, as a rule, as far from being thoroughly studied and having his condition properly diagnosed as he was following his first visit while the aggregate of fees paid totals a considerable sum. Professional work of this superficial and, unconsciously, dishonest kind is little removed from taking money from citizens under false pretense and through the legal protection of a medical diploma and license to practice medicine issued by the State Board of Medical Examiners. When one seriously considers that among the

patients thus superficially examined and treated there must be many who are suffering with the early and perfectly curable stages of certain diseases it makes us better realize the serious responsibility as well as the great privileges of our professional work.

I have often expressed the opinion to former classes that if every physician who is now practising his profession were thoroughly educated in medicine, was efficient in practice, and was diligent in his daily work, the men upon these benches would not find the welcome awaiting them from the public that they will surely find. There is scarcely a community in this country which is not ready to welcome a thoroughly trained physician. The medical graduate of this day is well educated and thoroughly trained and he lacks but one professional factor to make him successful, and that factor is experience, which he will acquire from day to day. You are better trained than previous classes, not because you proved yourselves better students or better men, but because the medical course improves each year as it continues to take advantage of all the improvements in the sister sciences.

A few years from now, I regret to prophesy, some of the men before me will have become examples of the careless physicians of which this and every other country has too many examples. Let me beg you to take the responsibilities of the profession seriously from the very beginning. Do your work in the college and hospital as well as you can train yourself to do it. Keep as closely in touch with the patients as your work will allow you to and use your books only as reference. Learn from those about you how to perform work better and learn equally from the mistakes and shortcomings of others what and what not to do. There is a successful professional future for every man who will play the game of life and of medicine squarely, and it is a comfort to know that if you try to do your best and attempt to make your best a little better each day you will be unafraid to have your work reviewed by any man. Now let me direct your attention to the more technical part of the physicial examination, and see if we cannot illustrate the helpfulness of such a routine.

In examining the eye, for instance, what practical points may the general practitioner note that will be helpful to him? We first note whether the eyes appear normal in external appearance. Is there exophthalmos present? is the conjunctivæ jaundiced? is there an arcus senilis present? are the pupils equal and do they react properly? is the cornea and the iris normal in appearance? is there present paralysis of the ocular muscles? is nystagmus present? Theoretically, at least, we will agree that to confirm such findings can do no possible harm and may prove of inestimable benefit to the patient. The time consumed is very slight and the record of the examination easily made.

How long does it take to inspect the pinnæ of the ears for gouty tophi and other abnormalities? how long to assure oneself of the condition of the internal ear? In these days of reasonably priced electric diagnostic ear and eye instruments there is little excuse for any physician not to avail himself of the opportunity for their use.

In the realm of pediatric practice it seems almost reckless to attempt to assume professional charge of a child without properly examining the throat, the ear, and the nasal cavities of the patient. So many hidden secrets are revealed by these simple examinations that one cannot afford to neglect them in a single case. There are far too many deaths resulting from unrecognized or too late recognized diphtheria cases, while the non-fatal cases often reach the hospitals or receive proper treatment at too advanced a stage to obtain the best results from specific therapy. It must be a rule without an exception that when we see a child for any illness whatever that is associated with fever that we will examine the throat, nose, and ear to assure ourselves of the normality of these organs. The examination of the mouth and throat of every patient who consults us is essential, but this is particularly true in infants and children. How often has inspection of the mouth revealed the cause of some supposedly mysterious illness to be due to such factors as thrush, erupting teeth, follicular tonsillitis, Vincent's angina, prodromal symptoms of measles (Koplik spots), noma, and similar easily recognized states. To examine the condition of the lips, the teeth, the gums, the

mucous membranes, the palate, the tonsils, the pharynx takes but a fraction of time, but is equally valuable time for the patient and for the physician. The latter is assured of a knowledge of normal conditions that are to be encountered, while the patient has the value of an expert inspection so that early or late pathologic changes may be recognized and corrected. There has been criticism of those who, according to their critics, have sacrificed "normal teeth and normal tonsils" in their too enthusiastic search for foci of infections. If one excludes the very slow and halting progress of education of the medical profession and the public to the beneficial effects of fresh air, good food, and rest in the treatment of pulmonary tuberculosis I know of no effort in education to be compared with the beneficial effects achieved in the recent crusade for an improvement in the hygiene of the teeth, nose, and throat. It is not to be denied that mistakes in judgment have been made regarding the necessity for the removal of both teeth and tonsils, but I believe far more good has been done in the way of preventive medicine than we can visualize just at this time.

To those who can remember the condition of the teeth, gums, and tonsils that were commonly encountered up to five years ago when we compare the greatly improved conditions of mouth hygiene today we can but feel that conditions have materially improved.

It is time well expended to assure oneself of the exact condition of the patient's mouth and throat hygiene, and it is certainly not sufficient, in many instances, to simply glance at the teeth or tonsils. It is imperative that even minor degrees of pyorrhea be discovered and corrected and that the pillar of the tonsil be retracted so that this organ can be thoroughly exposed to view. Tonsils that are diseased are too often the sole or, at least, the most potent factor in the etiology of certain cases of myocarditis, nephritis and arthritis, and other forms of focal infection for us to neglect a careful survey of these organs. To have the co-operation of a well-educated dental surgeon is indeed a great aid to a physician. No addition to the modern hospital has added more comfort and practical aid to the patients than the

presence upon the hospital staff of a corps of resident dental surgeons. One cannot but wonder that we attempted to exist so long without the close co-operation of this branch of the profession, for the results of their skill has long since proved how practical and helpful their presence in the hospital wards and dispensaries is. In the private practice of physicians it is equally important that there should be close co-operation between the dental surgeon, the dental hygienist, and the physician. The latter must acknowledge that the dental surgeon's special training and skill must make his judgment of matters connected with his specialty far more accurate and valuable than is the general understanding of the subject that is possessed by the physician. The best results are obtained for the patient when it is freely admitted that the two professions are dependent upon each other for mutual helpfulness.

What has been stated of the advantage to be obtained by consultations with dental surgeons is equally true of the good to be derived by using the skill of ophthalmologists. Here again the great advantage of routine measures are evident. One should complete a general examination *first*, and thus eliminate, as far as one may, any general cause for local symptoms, such as headache, neuralgic pains, and similar difficulties, but we should invariably have the special organs investigated by those competent to do so before we consider that we have given the patient every advantage of medical science. The particular point to bear in mind is that perfect health is too sacred a blessing to be, even potentially, sacrified because we, as physicians, failed to take advantage of every opportunity that might be helpful to the patient. To study our patients as carefully as we can is our duty, but it is no less our duty to encourage our patients to seek for special skill in certain lines that may be helpful to them. For patients whose incomes are limited it is always possible to aid them to receive expert opinions in the specialties at small or no cost, while those who are not limited in their expenditures can be referred to those whose skill can be purchased. Mutual obligations with our professional colleagues widens our views of medicine and increases materially our realization of how de-

pendent we are upon others for special skill and technical judgment.

It is well to make an invariable rule, especially in connection with so-called "nervous patients," to carefully examine the thyroid area by careful inspection and confirm our former opinion by palpation. It is especially helpful to palpate this area by grasping the thyroid area lightly between the thumb and finger and request that the patient swallow. It is surprising to find how frequently slight enlargement of the thyroid gland will escape observation unless this formal examination is adhered to. It is equally surprising to find how many patients are said to have an enlarged thyroid when, in reality, they have nothing palpable but a pad of fat in this area. It is not to be inferred that because a slightly enlarged thyroid is discovered that this is significant of disease, but if this or any other abnormality of the body exists it is well that their presence should be known and taken into consideration in estimation of the importance of the symptoms and signs present.

Well-developed forms of hyperthyroidism are easily recognized even by the unobserving, but the minor forms of this disorder commonly exist undiscovered for months and not infrequently for years. The same statement can be made with truth concerning hypothyroidism as well as with many other disease processes. As success in the treatment of most pathologic processes depends very much upon the discovery in the early stage of the nature and cause of the symptoms, it behooves all of us to study with great care our patients who have chronic illnesses and especially our "nervous" patients, that they may early have a correct diagnosis of their malady and may thus receive successful treatment. Not only will such unremitting care be helpful to the patient, but we as physicians and investigators will grow in skill in diagnosis.

The presence of scars of various kinds upon the cervical region is often an aid to diagnosis. The suggestive scars of the operation for drainage or removal of tuberculous glands may aid materially in the diagnosis of an obscure chain of symptoms, as will at times the symmetric scar over the thyroid area serve

to explain the less characteristic symptoms of hypothyroidism, myocarditis, nephritis, or some other sequel of a toxic goiter. A systematic palpation of the superficial lymphatic glands is a routine that must never be neglected. The anterior and posterior cervical chains, the axillary, the epitrochlear and the inguinal glands are worthy of thoughtful attention. The early diagnosis of lymphatic leukemia, Hodgkin's disease, lues, as well as the more common disorders of German measles, scarlet fever, tuberculous disease, and septic processes, can often be made if a routine examination of the glandular system is carried out.

The difficulties of making a correct diagnosis in the usual intrathoracic disease is frequently exaggerated in the mind of the physician who has not been in the habit of making routine examinations of his patients. If the examiner will but give himself the invaluable advantage of inspecting the uncovered chest in a suitably warm, well-lighted room it is amazing how helpful inspection may be in aiding in the diagnosis. It has been said that the most difficult part of the diagnosis was the difficulty encountered in persuading the patient to remove the chest clothing. There is truth in such a statement, but it is also true that many physicians make no real effort to have the patient disrobe, and until this is done the fault must lie at the door of our profession. It is our professional duty to educate the patients to the necessity for such thorough examinations, and it is detrimental to our profession to allow a patient to persuade us to treat his symptoms empirically without seriously attempting to learn the cause of the symptoms complained of.

To observe the contour of the chest, to note the equality or the difference in expansion of the two thoracic cavities, to note the depressions and pulsations in various areas of the chest, and to observe such deformities or abnormalities of the areas seen is most helpful. Too often the diagnosis is all too easily made, as patients frequently delay coming to a physician until diseased processes are well advanced. Can it be that our profession is partly at fault for this delay in consulting a physician? Is it because a patient with less obvious symptoms and signs receives little attention at our hands?

An aneurysm of the aorta may be difficult of diagnosis, as all experienced clinicians can affirm, but the average aneurysm is readily diagnosed if the patient is placed in a good light and the condition carefully searched for. To always remember to inspect the chest posteriorly may seem an unnecessary admonition, but when one remembers the aneurysms that have been discovered in this clinic pointing posteriorly, when we recall the angulations due to tuberculous processes in the vertebræ that were never seen or suspected, although the patient had long been under medical care, it will be well to mention the necessity of *complete* observation. Many a patient has been treated for pleurisy, intercostal neuralgia, lumbago, broken or bruised ribs, who upon inspection has been found to be suffering from herpes zoster, rickets, emphysema, kiphosis, lordosis, and scoliosis, all easily recognizable conditions upon inspection if the patient is undressed and examined.

Palpation is a great aid in confirming inspection, and the two forms of examination are commonly used simultaneously.

**Heart Examinations.**—The examination of the cardiac area by inspection and palpation is too often neglected. The accurate diagnosis of cardiac conditions by the average practitioner can be accomplished far more easily and accurately by the use of inspection and palpation than by auscultation, the method commonly, and I think mistakenly, adopted.

If one places the patient in a good light it is, as a rule, comparatively easy to ascertain the position of the apex-beat of the heart, and if this cannot be done by inspection alone, palpation or auscultation will confirm the finding. The change of posture of the patient is helpful in determining the position of the apex-beat and should be used in emphysematous or obese individuals. The cardiac apex-beat gives one an idea of the size of the left ventricle if we exclude the possibility of the heart being displaced by pressure from without. The palpation of the heart areas for the presence or absence of cardiac thrills is a distinct aid to accurate cardiac diagnosis. If there is a thrill present at the apex of the heart we must determine its position in the cardiac cycle by comparing the time of its presence with the apex-

beat. If the thrill occurs during diastole of the ventricles it is commonly due to either stenosis of the mitral orifice or to the regurgitation of the blood from the aorta into the left ventricle which abnormal blood-stream impinges upon the mitral valve leaflet, thus causing the thrill (Austin Flint thrill). We can diagnose or exclude aortic regurgitation by the presence or absence of the characteristic Corrigan pulse, the throbbing carotid arteries, and the presence or absence of the characteristic diastolic murmur over the body of the heart. We note the presence or absence of thrills over the base of the heart or in the vessels of the neck as well as the regularity or irregularity of the heart action.

We confirm our impression of the size of the heart by outlining the right and left borders by percussion, and use the same method in outlining the base of the heart in attempting to eliminate the possibility of aortic aneurysm.

If we have proceeded systematically we will have acquired an excellent idea of the nature of the cardiac lesion present if the heart is abnormal, and can then confirm the impression as to the nature of the lesion by auscultating the various cardiac areas for murmurs, altered heart sounds, pericardial friction sounds, etc.

The essentials for careful cardiac diagnosis are a practical knowledge of the physiology of the heart with a recognition of the common variations that occur within the realm of normal and a careful routine of examination for every patient examined. If a physician or student will devote himself as wholeheartedly to the examination of a normal heart as he does to an abnormal or diseased one he will very soon acquire judgment and skill in diagnosing the cause of the faulty mechanism in abnormal hearts. The difficulty with many practitioners, as well as many undergraduate students, is that they are uninterested in the methodic and complete examination of a normal heart. These same men find difficulty in differentiating a disorder of function from an organic disease of the heart because they do not possess a sufficiently elastic standard of comparison regarding "normal" organs. For the student or physician who would acquire special knowledge and skill in cardiac examinations and diagnosis

it is fundamentally important that he have or make the opportunity for examining the hearts of large numbers of individuals under greatly varying conditions. He should examine the hearts of infants and children both in health and disease, adolescent boys and girls when well and when suffering from various disorders, adults and aged people both in health and in sickness. The normal heart and the normal heart sounds can only be thoroughly appreciated by those who have enjoyed an extensive acquaintance with all the physiologic abnormalities of "normal hearts" and have formed an approximately correct impression of the variations that the term "normal" may include. There would be fewer errors in cardiac diagnosis were it a common custom for senior medical students and general practitioners to examine with care supposedly healthy boys and men in athletic clubs, gymnasiums, and similar organizations. The experiences of the medical departments of the various services during the late war illustrate how absolutely necessary it was to train the average physician in the special field of cardiovascular disorders and diagnosis of pulmonary disease. If we are to profit from the lessons of the war we must train ourselves to make more accurate diagnoses. One lesson, particularly emphasized by army experience, is that a heart should never be pronounced normal unless it is examined after exercise.

**Lung Examinations.**—Just as the knowledge of slight variation from normal is essential in cardiac diagnosis, so must one possess for correct diagnosis of lung conditions not only an understanding of the physiology of respiration, but of the various slight alterations from normal that are encountered in auscultating the breath sounds. An inspection of the behavior of the chest during respiration, when viewed both anteriorly and posteriorly, is quite as important as any other one method of examination. Inequality of expansion of the two thoracic cavities gives one a suggestion as to diagnostic possibilities, while retractions and pulsations indicate need for further examination. Palpation and percussion, if carried out systematically and routinely, are both helpful in themselves and of great value in conjunction with inspection and auscultation.

It is a very erroneous theory that percussion is an art that, once acquired, needs no practice. As a matter of fact, unless percussion is systematically and daily carried out in the most painstaking manner its findings are seldom to be depended upon. Gross changes in percussion a tyro can find, but slight percussion changes cannot be perceived unless one's fingers, one's ear, and one's brain are thoroughly trained to perceive them.

Our skill in interpreting what is heard upon auscultation depends very decidedly upon how familiar we are with normal breath sounds and their variations and our familiarity with the more or less physiologic sounds in the chest. Thousands of physicians have never recognized, as such, the grating sounds that result from the rubbing of certain articular surfaces together. It is not because these sounds are rare within the chest, but rather because when men hear them they often misinterpret them. Marginal râles also, that can be heard in any chest if carefully examined for, are, all too frequently, interpreted as pleural friction or as pathologic sounds. Muscle sounds and certain peculiarities of breath sounds, such as cog-wheel breathing, sticky crackles heard when patient swallows, distant feeble breathing, harsh breathing, etc., are interpreted in terms of pathology because the examination of large numbers of normal lungs has not been made.

Alteration of the normal breath sounds is a most important finding and helpful in aiding in the diagnosis, but we must be assured that the change is due to pathology and not due to a slight alteration in the physiology of breathing if we are to be correct in our judgment.

The presence of râles or adventitious sounds is an important finding in the chest, but a correct interpretation of the cause of the presence of such sounds is more important still. A râle is, after all, only a sound due to some alteration of the passage of air into or out of the air passages, and such sounds are very frequently due to obstruction in the upper air passages or in the larynx or trachea rather than in the lung itself.

It is good training for a student, young or old, to attempt to explain any physical signs encountered in terms of physiology

instead of pathology. Not only would students make fewer mistakes in their conclusions if such a plan was adopted, but clinical medicine would greatly improve as a result of the intensive study of the common physical findings.

The interpretation of any one physical sign must, of necessity, be based upon all the evidence in the case, *i. e.*, the history, the symptoms, the physical signs, and all the laboratory aid we can obtain. We will make mistakes in spite of all such precautions, but we will make less of them than if we attempt to make a diagnosis upon the presence of one symptom or one physical sign.

There is one precaution that it is wise to adopt before we conclude that a patient's lungs are free of râles, and that is to listen to the breath sounds of the patient, especially at the upper lobes, after the patient has exhaled the breath and followed this act by a single cough. Patients revealing persistent râles in such cases should be kept under observation and even more carefully studied with the aid of all laboratory help, such as blood counts, *x*-ray examinations, sputum examinations, etc.

**Examination of Abdomen.**—An examination of the abdomen of every patient that consults a physician should be considered essential to a correct understanding of the case. Just as it is necessary to be familiar with the appearance and feel of a normal chest, heart, and lung, so it is essential that we gain an idea of the average abdomen by examining a large number of abdomens under varying conditions of age, sex, musculature, etc., in healthy as well as in sick patients. It is essential for proper examination that the abdomen be bare. If this is not thought advisable, the nearer we can arrive at nudity the better for the examination. Inspection of the unclothed abdomen will, not infrequently, reveal a gastric tumor, a splenic enlargement, a pulsating liver, a distended bladder, and similar states not suspected by the patient and often overlooked by the attending physician. To palpate the abdomen may seem a simple act, but to do it well is one of the greatest arts in medicine. It is easy to palpate even a slightly enlarged liver or spleen if one has learned the knack of getting the patient to aid you, but many physicians never acquire confidence in their palpation findings

because they are not willing to routinely examine every abdomen as carefully as if they suspected the presence of pathology in this region. To carefully palpate the appendix area often throws light upon an obscure abdominal condition, a gentle palpation of the gall-bladder and liver area may suggest pathology. A gastric tumor may be palpated in time to save the patient much suffering from pyloric obstruction. The hernial rings can be carefully palpated and hernia of various kinds excluded as a causative factor in an abdominal case. Movable kidneys, hypernephromata, occasionally metastatic growths within the skin, as well as rose spots and various petechial hemorrhages, may be seen in an abdominal examination and give aid in an obscure condition.

The **examination of the sexual organs** is prone to be neglected, and in many cases it is imperative that these organs be examined as thoroughly as any other part of the body. Unsuspected urethritis, local lesions upon or about the genitalia, congenital deformities or abnormalities, tuberculous lesions of the epididymis, syphilis and malignant disease of the testicle, hydrocele, and hernia will often be overlooked to the detriment of the patient if the presence of such abnormalities are not discovered. It is almost equally important to examine the genitals of a female in any obscure or complicated condition. There can be no good reason why such an examination should not be made, and in many instances symptoms having apparantly remote connection with the genital apparatus have been found to be due to diseases of the genital apparatus. Any physician in general practice must familiarize himself with the normal findings of vaginal examinations, and certainly no abdominal condition can be said to have been completely examined unless a vaginal or rectal examination has been made.

**The Neurologic Examination.**—A general practitioner cannot be expected to know all the refinements of neurologic examinations, but it is not too much to expect him to test the ordinary superficial and deep reflexes.

That these are practical examinations and save serious errors there can be no doubt. Too many tabetics are still treated for

"indigestion" and too many bear the scars of having their abdomens opened under suspicion of having gastric ulcer and other surgical conditions of the upper abdomen. To test a knee-jerk is simple and not time consuming and often very illuminative in diagnosis. A Babinski test is easily performed and is equally helpful in a differential diagnosis. To test for pain sensation often throws light upon otherwise obscure conditions.

To test for rigidity of the neck in all febrile cases, especially in those cases complaining of headache, will make for earlier thought of the diagnosis of meningitis and possibly for the saving of life in this condition. The presence or absence of Kernig's sign is useful in determining the true nature of obscure nervous symptoms.

A lumbar puncture should be a routine procedure in all obscure nervous cases. A great deal can be learned in this way that would otherwise be difficult or impossible to learn. Although it is not, as a rule, necessary, a sensitive patient can be lightly anesthetized for this operation and thus avoid the criticism of unnecessary pain having been caused. The operation should be done early instead of late, and every physician in general practice should be able to do this simple and useful operation. A correct early diagnosis in meningitis is the first step toward recovery, and the test is equally helpful in a number of other conditions.

**Blood Examinations.**—In every obscure illness, and such disorders are more common than are easily diagnosed conditions, there should be a complete blood count made, including a differential count.

The well-known fact that this is relatively seldom done outside a hospital does not change the truth of the above statement. Help that can be found in no other examination will be found not infrequently, and even when the result is not decisive, one is a better trained physician if he can make a relatively accurate blood count.

Pernicious anemia, myelogenous and lymphatic leukemia, splenic anemia, lead-poisoning, and the various forms of secondary anemia can be more intelligently diagnosed and treated if

we are willing to take the time to make or, if we do not wish to examine the blood ourselves, have made for us by those who are more particularly laboratory workers. A leukocyte count is easily made, takes but little time, and often its result is a most valuable and decisive aid in making a differential diagnosis. Eosinophilia is commonly encountered and frequently leads to a correct diagnosis being made. Basophilic degeneration of the red cells in the absence of any other well-known cause of this condition makes one suspicious of chronic lead-poisoning and the closer study of the case often confirms the suspicion.

Every chronic illness should call for a Wassermann test of the blood. We do not expect to find but a small percentage of the cases examined positive, but the test should be made in order that we may have the great benefit of either a positive or a negative reaction. We do not expect to find sugar in the urine except in a small percentage of the urines that we examine, but we feel that it is well to rule out the possiblity of the presence of sugar, and we should consider the Wassermann test in the same light. A positive test calls our attention to the possibility of a luetic infection, and although there is always present a possibility of error in the laboratory technic, as in all such tests, it is well to have our attention directed to the possibility of an ancient or more recent syphilitic infection. The discovery of such an infection is a most important aid in selecting proper therapy.

**Urine Examinations.**—No physical examination of a patient should be considered complete unless a urine examniation is performed. This may not seem to be an essential part of the examination, but when we consider that it is the most direct method of ascertaining the state of such a vital organ as the kidney, the necessity and importance of the examination is clear. One does not require an elaborate laboratory to examine a urine with all the thoroughness that is usually necessary. A Bunsen burner or an alcohol lamp, a few test-tubes, a bottle of acetic acid, Fehling's or Benedick's solution, filter-papers, funnels, glass slides, and cover-slips, a specific gravity jar and urinometer, sedimenting tubes, and a microscope are the most essential equipment. A centrifuge is unnecessary if one uses the

sedimenting glasses which are perfectly satisfactory. Tests for albumin, sugar, casts, and other urinary sediments should be performed in every case, and if one is suspicious because of symptoms that the patient has a nephritis, pyelitis, or similar condition frequent examinations at intervals should be performed.

The number of cases of unsuspected pyelitis, cystitis, hematuria, and nephritis that will be diagnosed if routine methods of examination are adopted is surprising. This statement is equally true when applied to diabetes. The tests are so simple, take so little time, and are so potentially valuable to the patient, the physician, and to the medical profession that there is no legitimate excuse for the neglect of such a fundamental and basic portion of a diagnosis.

**Rectal Examinations.**—In any hospital that draws its patients from far and near there is always an opportunity for profiting from the mistakes in diagnosis that are discovered by routine examination of referred patients. I wish to warn you very particularly about the necessity of making a routine rectal examination in every patient that complains of chronic abdominal symptoms. Rectal examinations may not seem particularly pleasant to make, but we must always remember that such an examination is even more unpleasant to the patient.

Familiarize yourself with the normal conditions to be found in a rectal examination in the male and female patient by examining all patients that complain of abdominal difficulties. After a correct idea of the normal variations encountered in such examinations is obtained the correct interpretation of pathologic states is easily made. One dislikes to think how often fistula in ano is diagnosed "piles," and how frequently carcinoma of the rectum is undiagnosed for lack of a proper examination.

Rubber gloves are not expensive, proper lubricant easily obtained, and a rectal examination neither difficult nor painful. Let us resolve that we will not neglect a careful study of rectal symptoms. It has been said by a celebrated Philadelphia surgeon that in obscure cases of abdominal disease that, not

infrequently, during the routine rectal examination "the diagnosis jumped on to his finger."

**The Roentgen Ray Examination.**—This valuable addition to the armamentarium of the medical and surgical diagnostician can be classed as a most valuable form of inspection. Were it not for the expense involved in its use, expense not only in the price of the apparatus and accessories, but in the years of training necessary in its proper use, this method would be a most useful adjunct in every physician's office.

The roentgenologist is the most helpful consultant in many of our most obscure medical and surgical maladies and can quite often aid us when other means fail.

We should carefully consider in any obscure condition whether the use of the Roentgen ray would not give us help and refer the patient in time to have them receive the information available much earlier than is sometimes done.

Ulcers, strictures, abnormalities, and malignant growths of the gastro-intestinal tract; renal stones, tumor, pyonephrosis and other pathologic states of the kidney; abscess, foreign bodies, empyemata and other abnormal conditions of the lungs; fractures, deformities, growths and anomalies of bones and joints are among the numerous conditions that can be more easily and more correctly diagnosed with the Roentgen ray than by other methods.

I have mentioned a few of the more important examinations, from the standpoint of a clinician, that should be made as a matter of routine. Other examinations, scarcely less important, will occur to all of you. The basic truth and idea upon which this lecture is given is that in becoming a physician we, each of us, obligate ourselves to conduct our lives in accord with the ideals of the medical profession.

No matter how hard we try we shall, at times, fall short of those ideals, but the more nearly we attempt to approximate the spirit of the Golden Rule in our professional lives, the happier we will be and the more useful citizens we will become.

Dire prophesies are heard in these days concerning the ultimate taking over of the practice of medicine by the State in

connection with the proposed plan of National Health insurance.

Such a consummation would be, in my opinion, a calamity for the nation as well as for our profession. We must bear in mind, however, that if the general public invariably received the highest grade of medical services that all physicians can train themselves to give there would never be a demand for such a plan. It is the inefficiency of much of the medical work performed by a certain grade of practitioner that causes wide-spread dissatisfaction and desire for a change of method.

If each of us resolve that we will give our best efforts at all times to those who seek our aid, and if we live up to our resolve, our patients will be indeed fortunate. Our responsibility does not cease when we have completed our examination. We must be interested enough to study our patients, consult standard books, read the current literature, and make a serious attempt to carry on postgraduate instruction in our daily work with our patients. If one does not progress in medicine one retrogrades. Let us be among those that are alive to every aid for our patients and thus deserve an honorable position in our chosen profession.

## CLINIC OF DR. C. C. WOLFERTH

From the Cardiovascular Clinic, Medical Out-patient Department, University Hospital

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# ABNORMAL CARDIAC RHYTHMS AND THEIR DIFFERENTIATION BY SIMPLE METHODS

I wish to present to you today two patients who illustrate certain phases of the subject of abnormal cardiac rhythms, and then discuss the differentiation of arhythmias by simple methods of physical examination.

### CASE I

This girl, C. N., nineteen years old, presents one of the commonest conditions you will be called on to manage. In 1906, when she was five years old, she had an attack of acute articular rheumatism. After her recovery her family noticed that she was short of breath on exertion. The breathlessness improved gradually, and she then felt well until 1915, when she had a second attack of rheumatism. During this attack her heart beat very fast. The joints cleared up after a few weeks, but the rapid heart action persisted and she had pain under her left breast.

In 1916 she appeared in the Medical Out-patient Department, complaining of shortness of breath, cough, and headache. At that time it was noted that the heart was moderately enlarged, there was a systolic thrill and murmur at the apex, and an accentuated pulmonic second sound. The rhythm was regular. She came to the Out-patient Department for six months and finally improved enough that treatment was discontinued.

About a year ago she again presented herself, complaining of shortness of breath. She was referred to the Cardiovascular Clinic, where she has been under observation ever since. In

the interval since 1916 she had been in poor health most of the time. There had been a number of attacks of digestive disturbances, and at one time she was thought to have had acute appendicitis. She had not been able to work since 1917 because of rapid heart and breathlessness. She had also had frequent attacks of bronchitis.

On examination, she was slightly cyanotic and orthopneic. The heart was markedly enlarged, the right border extending out 6.5 cm. from the midsternal line, while the apex impulse was found in the left anterior axillary line. A diastolic thrill and murmur were noted at the apex in addition to the systolic, evidencing that mitral stenosis had developed since her previous visits. The cardiac rate was very rapid, the rhythm totally irregular, and there was a large pulse deficit.

You will observe that today she shows no cyanosis or evidences of breathlessness, in fact, looks quite well. She states that recently she has felt better than any time since her attack of rheumatism seven years ago. She no longer suffers from shortness of breath, precordial pain, cough or gastro-intestinal symptoms, which had troubled her almost constantly.

I want one of you who has examined her to describe her cardiac rhythm.

STUDENT: The pulse is irregular.

DR. WOLFERTH: Don't get into the habit of describing a pulse as irregular and let it go at that. You should observe particularly whether the irregularity is continuous or only occasional, whether there is a total absence of rhythm or some type of regularly recurring irregularity can be made out. A second criticism is that your observations should be based on auscultation of the heart rather than the pulse alone, as the latter may mislead you. Listen to the heart again and then tell me what you have observed about the rhythm.

STUDENT: There seem to be periods of regularity and then short periods of irregularity.

DR. WOLFERTH: What about the rate?

STUDENT: It is 74 by auscultation, but a few beats have no pulse accompanying them.

DR. WOLFERTH: What do you call such a condition?

STUDENT: Pulse deficit.

DR. WOLFERTH: Yes. Now have her walk across the room rapidly several times and tell me if you note any changes.

STUDENT: The rate has increased and the irregularity seems to be continuous.

DR. WOLFERTH: What do you think the disturbance of rhythm is due to?

STUDENT: Auricular fibrillation.

DR. WOLFERTH: Yes, the case is a fairly typical one. On your recognition of the fibrillation will depend your success in treating this very common condition. Her heart is now under the influence of digitalis which is largely responsible for her present rate around 70. Not infrequently under such circumstances there may be an almost regular rhythm such as she showed, so that you may be in some doubt as to the nature of the disturbance unless you increase the rate. Noting the behavior of the heart action as the rate is increased is the most important procedure in helping to decide whether the condition is fibrillation or not. When this girl's rate was increased to 120 it became quite evident that the rhythm was totally irregular or, strictly speaking, there was no rhythm. You could then feel fairly confident that she had auricular fibrillation. What else might it be?

STUDENT: Auricular flutter.

DR. WOLFERTH: Yes, seeing her today for the first time, with a heart action that seemed to you to show at times elements of regularity, you would be justified in thinking of flutter. But I do not agree with you that the rhythm is quite regular at times. I think a careful examination will show you that there is a slight continuous irregularity in the intervals between the grosser disturbances. Furthermore, she has been under observation and treatment here for a year; in that time she has never had a regular rhythm during any of her visits. Flutter is rare compared with fibrillation, particularly the type with apparently totally irregular heart action. The clinical differentiation may be impossible. Transitional forms are found that we have not yet learned

to differentiate by electrocardiographic study. The recent experimental work of Lewis has shown how closely flutter and fibrillation are related. He obtained electrocardiographic tracings in animals simulating fibrillation, but which, he has demonstrated, are in reality due to flutter in which the spread of the wave of excitation to contraction through the auricle has been modified. The safest clinical rule to follow is to regard the cases with totally irregular ventricular action as fibrillation until you can exclude it. Your diagnosis will nearly always be correct and the effectiveness of your treatment will depend more on other considerations than whether the disturbance of the cardiac mechanism is to be regarded as flutter or fibrillation.

Numerous electrocardiograms of this patient have always shown auricular fibrillation. The fluctuations of the heart rate have been of some interest. So long as she has faithfully followed instructions and at the same time been able to avoid bronchial infection her pulse-rate has stayed near 70 and she has been in comparatively good health. She has been given digitalis almost constantly lately, in the form of digitan, which she prefers to the tincture of digitalis. About 0.1 gm. per day, sometimes a little more, sometimes a little less, has been necessary to maintain her present condition. Once she went away for a month, took no digitalis for over three weeks, and disregarded instructions as to hygiene and exercise. When she returned her heart rate was 170, there was a large pulse deficit, and she was markedly decompensated. Twice attacks of bronchitis have been followed by similar conditions.

### CASE II

This man, sixty-three years old, has presented more complex conditions than the girl you have just seen. His record is as follows: He was perfectly well until 1914, when he began suffering from frequency of urination, which increased until a prostatectomy was performed in July, 1918. About six months after the operation he began to suffer from discomfort and distention after eating, and constipation, also palpitation of the heart, which would sometimes wake him at night. He thinks

his heart did not beat any more rapidly than usual during the periods of palpitation.

Because of these symptoms he presented himself at the Outpatient Department in December, 1918. The examination at that time showed no cardiac abnormalities, the liver extended just below the costal margin. The blood-pressure was 136–78. The heart rhythm was noted as regular, and the pulse was counted on one examination as 65 and on another as 75. Treatment was directed mainly to the gastro-intestinal tract; antacids, belladonna, and mild sedatives were given. After a few visits he was very much improved and did not return until August, 1919, when he again complained of palpitation and excessive gas after eating. He again improved following a dietary régime—belladonna and silver nitrate.

On October 2d, after having been away for five weeks, he came in stating that for two weeks he had been very short of breath and weak and that his pulse had been very rapid. On this visit he was referred to the Cardiovascular Clinic. Examination showed no visible abnormal pulsations in the neck, no cardiac impulse was palpable, percussion outline of the heart was about normal, and no murmurs were heard. The cardiac rate was rapid, the rhythm was sometimes nearly regular (regular periods interrupted by occasional slight irregularity), at other times grossly irregular. With the former type of rhythm the rate was approximately 135. When he lay down the rate decreased and the rhythm was of the grossly irregular type. On mild exertion the rhythm became almost perfectly regular again, but the rate did not exceed 135. A distinct pulsus alternans was obtained during periods of regular action both by palpation of the radial artery and by auscultation over the brachial while the blood-pressure was being taken.

The electrocardiogram taken that day showed perfectly regular auricular rate of 272, and for the most part a ventricular rate of 136, which shows occasional slight irregularity in the interventricular intervals (Fig. 125, tracing 1). You will observe the characteristic diphasic oscillations due to the continuous auricular activity of flutter, and that one ventricular complex is

found to two auricular, evidencing what is called a 2 to 1 block, the relation found most frequently in untreated flutter. In view of the perfectly regular auricular rhythm one should naturally expect the ventricular to be equally regular. Nevertheless, not infrequently slight irregularity is found which may be due to alterations in conduction between the auricles and ventricles.

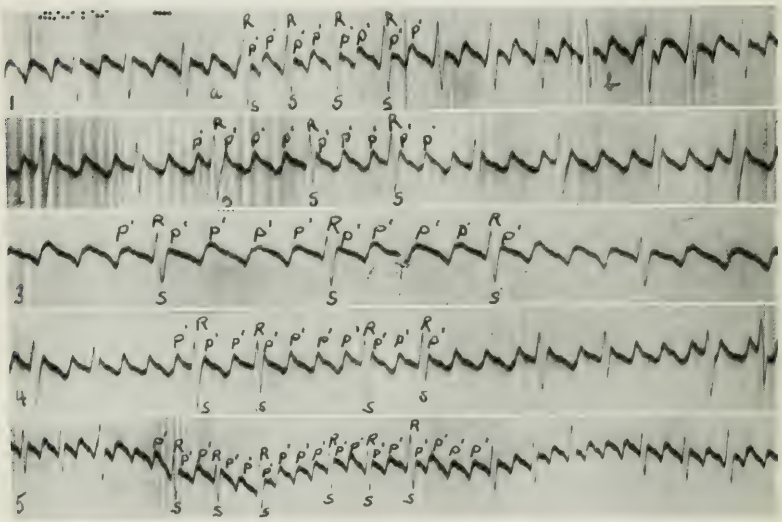

Fig. 125.—Case II. Auricular flutter with types of ventricular action that clinically seemed to show at least some regularity. Tracing 1: After the first ventricular complex, there are two auricular contractions to one ventricular. The rhythm is not quite regular; at *a* and *b* the interventricular period is somewhat lengthened and the next succeeding one correspondingly shortened, so that the two periods equal in time two ordinary cycles. Tracings 2 and 3 respectively are examples of 3 to 1 and 4 to 1 rhythm; clinically, they appeared perfectly regular and by measurement there is very slight irregularity. Tracing 4: Coupled beats in flutter (alternate 4 to 1, 2 to 1 auricular-ventricular contractions). Tracing 5: "Tripled" beats in flutter (4 to 1, 2 to 1, 2 to 1 auricular ventricular contractions).

He was given tincture of digitalis, 1 c.c. q. i. d., and advised to stay in bed most of the time until his next visit. Five days later he returned saying that he felt much better. His rate was now slow, but the regular dominant rhythm was interrupted by numerous extrasystoles which were easily abolished by mild

exertion. The electrocardiogram showed a sinus rate of 48, interrupted by numerous extrasystoles, arising from at least one auricular and two ventricular foci. The digitalis was discontinued, but the next week he returned feeling much worse and the flutter with 2 to 1 rhythm was found to be re-established. He was sent into the ward, where he remained three weeks. He was again given digitalis. The 2 to 1 block was converted into 3 to 1, a form that is comparatively rare. Then a curious alternating 4 to 1, 2 to 1 block, that simulated pulsus bigeminus, was obtained. At times there were periods of apparent irregular irregularity. Eventually there was a regular 4 to 1 block which could be easily disturbed by changes of posture or exertion. The flutter continued during his entire stay in the ward. The auricular rate remained remarkably constant, the widest variation being from 272 to 286 during a period of over three months' observation and in two separate attacks; it was apparently unaffected by exercise, vagal stimulation or digitalis, and the slowest auricular rate was obtained before digitalis treatment was instituted.

He left the hospital January 8, 1920 improved, but the flutter was still present. Five months later he reported one day with the story that for about a month after leaving the hospital his condition had remained about the same and he had been bothered a great deal by palpitation and distention after eating. One day he drank a bottle of home-brew beer of reputed high alcoholic content, the first alcohol he had taken since his illness. Within a few minutes the rapid heart action and the palpitation disappeared and up to the present have not returned. On examination, the improved appearance was striking, he had gained 8 pounds, the cardiac action was slow and regular. An electrocardiogram showed normal sinus rhythm.

Today, just about a year from the time his auricular flutter was discovered, he returns, saying that again he is troubled with discomfort after eating and is somewhat short of breath on exertion.

(To student who had examined patient): How would you describe his cardiac rhythm?

STUDENT: It is totally irregular and the rate is about 130.

DR. WOLFERTH: What was the effect of exertion?

STUDENT: The rate increased and the total arhythmia persisted.

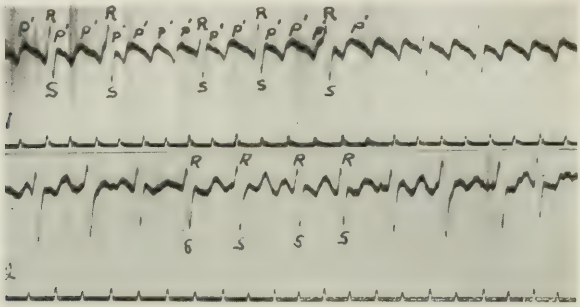

Fig. 126.—Case II. Types of clinically total irregularity. Tracing 1: Auricular flutter. Not only are the number of auricular to ventricular contractions changing irregularly, but the relation of the ventricular contraction to its preceding auricular contraction is also constantly shifting. Tracing 2: Obtained on patient's last visit. Total irregularity due to auricular fibrillation.

DR. WOLFERTH: Did you note any periods of regularity?

STUDENT: No.

DR. WOLFERTH: What do you think the present disturbance of rhythm is?

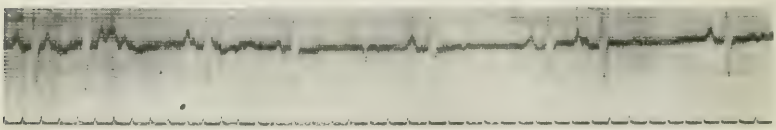

Fig. 127.—Case II. Total irregularity due to numerous extrasystoles of both auricular and ventricular origin. Five days before had shown 2 to 1 auricular flutter and during the interval had taken 1 c.c. tincture of digitalis q. i. d. The irregularity was completely abolished by increasing the rate of the dominant rhythm to 60.

STUDENT: It seems like auricular fibrillation.

DR. WOLFERTH: Yes. But in view of the previous record of flutter and marked pulsus alternans one should be suspicious of flutter even though the heart action seems totally irregular

and wide irregular variations in pulse volume are found; otherwise it would scarcely be thought of at present. I am unable to exclude it absolutely by physical examination. But the electrocardiographic film just taken shows that the present condition must be regarded as auricular fibrillation.

This patient has shown certain of the features often observed in connection with flutter, such as the effect of digitalis in increasing the auriculoventricular block with consequent slowing of the ventricular rate; the variety of ventricular action dependent on the block; the pulsus alternans when the ventricular rate was rapid; the presence of numerous auricular extrasystoles shortly after sinus rhythm had been re-established; and finally, the development of auricular fibrillation. On the other hand, the typical sequence of events, namely, auricular flutter, auricular fibrillation, normal sinus rhythm following the use of digitalis, was not observed, although possibly it may have occurred.

## THE DIFFERENTIATION OF ABNORMAL CARDIAC RHYTHMS BY SIMPLE METHODS

With the advent of the electrocardiograph and the consequent clear-cut classification of abnormal cardiac rhythms, making possible the clinical study of each type, the field of clinical diagnosis has been so far extended that anyone sufficiently interested can easily recognize, by simple methods, the nature of the disturbance in the vast majority of patients with abnormal cardiac rhythm. Since graphic methods of study are out of the question for many patients, it is important to become expert in differentiating these disturbances of rhythm by simple methods that require no complicated apparatus. The data from which conclusions may be arrived at are easily gathered, while control electrocardiograms show that it is possible to reach a much higher degree of accuracy than is usually attained in clinical diagnosis.

Fortunately, the three commonest types of arhythmia—sinus arhythmia, extrasystoles or premature contractions, and auricular fibrillation—are the easiest to recognize. At the other end of the scale the very rare types, such as auriculoventricular

rhythm, certain forms of idioventricular rhythm (excluding complete heart-block), and sino-auricular heart-block, although they may be recognized as abnormal, cannot be diagnosed clinically; they are usually taken to be some form of auriculoventricular heart-block. The disturbances of conduction that do not alter the rhythm, such as simple delay in the transmission of the impulse to contraction through the bundle of Kent (His), or block in one of the branches of the bundle or in the terminal arborizations, with one rare exception,[1] do not furnish clinical evidences sufficient for their recognition.

In the study of a case of suspected abnormal cardiac rhythm the character of the rhythm should be carefully noted; whether or not there is any irregularity, and if so, whether the irregularity occurs only occasionally, is frequent or continuous. When the irregularity is considered continuous, it should be decided whether the arhythmia is total or recurring cycles of the same irregularity are discoverable.

The method of estimating disturbances in the rhythm should be auscultation of the heart sounds rather than palpating the pulse. Auditory perception of rhythm is more acute than tactile, but more important is the fact that the pulse does not always completely reflect the cardiac action. The pulse should always be studied carefully, and it often yields information of the greatest value. But it should occupy a subsidiary position as a means of grouping cardiac rhythms as a confirmatory test of auscultatory findings.

The study of the cardiac rate is second in importance only to the rhythm. The behavior of both rate and rhythm under various circumstances, such as change of posture, exercise, vagal stimulation, atropin injection, often furnishes information that leads to a correct conclusion as to the nature of the disturbance.

Perhaps the simplest method of attacking the problem of the differentiation of the arhythmias that may be recognized clin-

[1] The exception is found occasionally where there is delay in the transmission of the impulse from auricle to ventricle in a heart with mitral stenosis. As delay in conduction develops the relation of the presystolic murmur to the first sound is observed to change.

ically is to classify cardiac action according to its regularity as determined by auscultation, namely, (1) regular cardiac action, (2) partially irregular cardiac action, and (3) totally irregular cardiac action. Thus the problems that arise in each of these groups may be considered separately.

**Regular Cardiac Action.**—When the rhythm is regular, abnormal cardiac mechanism (excepting pulsus alternans) would rarely be suspected unless the rate is either abnormally slow or rapid. In the former heart-block is to be considered, in the latter paroxysmal tachycardia or auricular flutter.

When the rate is under 60 the possibility of high grade of heart-block should suggest itself—the slower the rate, the more probable the presence of block. With a rate under 40 normal or sinus rhythm is rare. In complete block[1] the rate is most often around 30, although it may be much slower; it is rarely over 45. It is distinguished from sinus rhythm by the fact that changes in posture or exercise cause little if any change in the ventricular rate, while atropin injection is entirely without effect except in functional complete block such as that produced by drugs, where it may lessen or completely abolish the block, with the production respectively of incomplete block or sinus rhythm. In the latter event the rate would be augmented to the normal or even higher.

Very high grades of incomplete block (3 to 1, 4 to 1) are very rare; it is not necessary to differentiate them from complete block, as they tend to pass into that condition. They are usually characterized by very slow ventricular action.

It is sometimes difficult to differentiate 2 to 1 block from slow heart action of the normal type unless by some procedure, such as change of posture, exercise or atropin, we are enabled to change the grade of block or abolish it. The development of irregularity as the rate is increased points very strongly to incomplete block. In any event, it serves to show that the cardiac mechanism is abnormal.

[1] The ventricular rhythm in complete heart-block is often slightly irregular, but owing to the slow rate this is not appreciated clinically. Occasionally the ventricular action is grossly irregular.

When the ventricular rate is slow examiners thoroughly familiar with venous pulse curves may often obtain valuable information from observing the waves in the neck. This method is not recommended for those not versed in cardiography, as too often it will be confusing and lead to error.

If the rate is between 70 and 140, it might be possible, under exceptional circumstances, to recognize auricular flutter. A history of sudden onset or sudden increase of symptoms referable to the heart, particularly palpitation, should lead to the suspicion of this condition. Flutter with regular ventricular rhythm, owing to the practically fixed auricular rate, presents certain characteristic features that depend on the associated heart-block. Thus, if the auricular rate were 300, we might expect to obtain regular ventricular rates of either 150 (2 to 1 block), 100 (3 to 1 block), or 75 (4 to 1 block). All intermediate rates must necessarily be at least partially irregular. Consequently, if either decrease or augmentation of the rate can be produced by such procedures as change in posture or exertion, irregularity is prone to develop. One does not find gradual decrease of the rate of a dominant rhythm such as occurs with a normal heart after exercise.

When the rate is approximately 140 or more the problem consists of the differentiation of simple or sinus tachycardia, paroxysmal tachycardia, and auricular flutter. It is rare to find such a rapid simple tachycardia without some evident cause for it, such as infection, toxemia, nervous or psychic condition. It is rare even in severe heart disease unless there is some added factor such as one of the conditions mentioned.

Paroxysmal tachycardia is characterized by sudden onset and offset, usually appreciated by the patient, the constant rapid rate usually between 140 and 220, the insusceptibility to change with change of posture, exercise, emotion, or atropin. Vagal stimulation will bring about cessation of the paroxysm in approximately 50 per cent. of the cases, but does not influence the rate of the paroxysm. This artificial cessation of the paroxysm may be considered pathognomonic of paroxysmal tachycardia,

since, according to Ritchie, it will not stop an attack of auricular flutter.

Up to the past few years auricular flutter with rapid regular rhythm was not distinguished from paroxysmal tachycardia, and until very recently the dividing-line between the two conditions was not considered a very sharp one. It is now thought that the mechanisms of the two conditions are quite different. The clinical differentiation is not always clear, but certain points may be of value. Paroxysmal tachycardia frequently develops in otherwise apparently undamaged hearts; flutter rarely. In the former there may be a history of many brief attacks for years without much embarrassment to the patient except during the attack; such a history would be unusual in flutter, as the latter tends to establish itself for longer periods and not to recur frequently in brief attacks.[1] During the attack the cardiac action nearly always remains regular in paroxysmal tachycardia, except for a rather rare occasional dropped beat. In flutter, change of posture, mild exertion, such as walking across the room or vagal stimulation, will frequently change the ventricular rate, also the rhythm. Digitalis in ordinary dosage usually slows the rate of flutter and may convert the mechanism to auricular fibrillation; it has no effect on paroxysmal tachycardia except that occasionally it seems to have some relation to the cessation of a paroxysm.

**Partially Irregular Heart Action.**—Among the partially irregular rhythms may be included those showing varying grades of irregularity, ranging from an infrequent disturbance of the rhythm to continuous irregularity, but in all of which at least some element of regularity is discoverable. This is the group in which the vast majority of the arhythmias are placed, due to the fact that nearly all cases of sinus and extrasystolic arhythmia must be included. The former is so frequent in childhood and adolescence as to be considered physiologic, while at least occasional extrasystoles are very frequent in later middle life and almost universal in old age.

Sinus arhythmia may nearly always be recognized by atten-

[1] Lewis mentions a case in which the flutter lasted for six years.

tion to the character of the irregularity. In most cases the changes are coincident with the phases of respiration, usually quickening during inspiration and slowing during expiration, although occasionally the opposite may be found. The changes are often exaggerated by deeper breathing. There is another type independent of respiration in which the cycles of irregularity are less frequent. In these cases there is also found the waxing and waning of the rate characteristic of this rhythm. The arhythmia is easily abolished by lessening of vagal tone such as can be produced by mild exercise or atropin. It is rarely found with a rate over 120, although occasionally it has been noted with a rate as high as 140.

Extrasystolic arhythmia is protean in its manifestations; it may vary from a single premature beat recurring at very long intervals to irregular contractions arising from multiple foci throughout the heart and far outnumbering the contractions of normal origin. This latter form will be considered under totally irregular rhythms. The chief characteristic of extrasystole is the prematurity of the beat disturbing the rhythm; it always occurs before the next normal beat would be expected. It may or may not be followed by a compensatory pause; occasionally it does not even disturb a slow normal rhythm, being merely interpolated between two contractions of normal origin.

Experience in the auscultation of hearts will often enable the examiner to recognize an extrasystole by the character of the sound. The extrasystolic first sound is usually sharp and lacking in the so-called muscular element. The two sounds often seem closer together than the normal sounds. Sometimes they are muffled and weak. Not infrequently the aortic valve is not lifted, so that only a first sound is heard. In this event there is, of course, no pulse at the wrist, as occurs sometimes even when the second sound is heard. When a pulse accompanies an extrasystole it is weaker than the normal pulse.

Extrasystoles are usually most numerous when the rate is slow or around normal. As the rate is increased by any cause they tend to disappear, so that in most cases they are abolished with a rate of 120 and are extremely unusual with a rate of 140.

Very rarely, as the rate is increased, the number of extrasystoles also increases, in which event they are considered to indicate serious myocardial disturbance.

Occasionally the differentiation must be made between extrasystoles without corresponding wrist pulse and with abolition of one cardiac cycle of the dominant rhythm, and dropped beats due to partial heart-block. Usually the dropped beat recurs more regularly than extrasystole; every third or fourth beat, etc., may be dropped for fairly long intervals, but with very slight grades of block there may be no regularity in respect of the dropped beat. The principal difference between the two conditions lies in the fact that in block instead of a premature beat followed by either a compensatory pause or immediate resumption of the regular rhythm, there is found silence over the heart during a period almost twice as long as the normal interval. In extrasystolic arhythmia, as stated above, the arhythmia is nearly always diminished by increasing the rate; in block, the number of dropped beats is frequently increased.

Auricular flutter, which would be a bugbear in clinical differentiation except for its relative infrequency, sometimes presents itself as a partially irregular rhythm. One is likely to find periods of regularity alternating with periods of irregularity. Occasionally there seems to be a dominant rhythm interrupted by premature contractions; even the form of extrasystolic arhythmia called pulsus bigeminus may be simulated (Fig. 125, tracing 4). The differentiation from extrasystoles cannot always be made with certainty, but observation of the reaction to exercise may help. In flutter one is not able to obtain numerous variations in rate of the dominant rhythm on exercise, nor is abolition of irregularity as the rate is increased and gradual return as it diminishes again so liable to be found. The auscultatory peculiarities of extrasystole may also help in the differentiation.

Auricular fibrillation must also be mentioned in this group, as it sometimes seems to show a regular dominant rhythm interrupted by occasional irregularity, thus resembling extrasystoles. This condition is most frequently found after digitalis administration. Exact measurements would show a continuous irreg-

ularity, but auditory perception is not always keen enough to recognize it. The differentiation from extrasystole is usually easy enough if one is on the lookout for fibrillation. Increase of the pulse-rate tends to abolish extrasystoles, whereas in fibrillation the irregularity is not abolished, but is usually increased and the simulation of a dominant rhythm disappears.

**Totally Irregular Heart Action.**—When the cardiac rhythm appears totally irregular the overwhelming majority of cases are found to have auricular fibrillation, but there are certain exceptions that must be borne in mind. When the rate is under 100 cases showing frequent extrasystoles, especially where they are arising from various foci, may present totally irregular rhythm. Perhaps the most frequent error and certainly the most important one encountered is mistaking the totally irregular rhythm of auricular fibrillation for extrasystolic arhythmia. This mistake should not be made if one always thinks of auricular fibrillation in connection with any gross irregularity. Again, the differentiation must be made by increasing the pulse-rate; if the gross irregularity persists the arhythmia is due to fibrillation rather than extrasystoles.

There is an extremely rare type of arhythmia, classified as a sinus arhythmia, in which there is a total irregularity. The rhythm is said to become regular as the rate is increased. On account of its rarity it is of little practical importance.

Flutter may present an apparently total irregularity, although Lewis has shown that measurements of grouped beats, so-called spacing, shows an element of regularity. With a rate over 100 this is practically the only condition that simulates fibrillation. It is usually difficult and sometimes impossible to distinguish the two conditions. From the standpoint of the patient this makes little difference since the underlying mechanisms are undoubtedly closely related, the prognosis is similar and the treatment, with minor differences in the administration of digitalis, the same.

**Pulsus Alternans.**—The conditions we have discussed have to do with abnormalities in the formation, point of origin, or the spread of the impulse to contraction. Pulsus alternans is

thought to be a different process. It is generally held to evidence a disturbance in the function of contractility. As the name indicates, it is characterized by alternate larger and smaller pulse waves.

As has been pointed out by several investigators, notably by White, alternation occurs oftener than was formerly supposed and is found frequently in myocardial disease, especially cardiorenal disease, if carefully looked for. For purposes of convenience it may be classified as latent and developed. In the former there is a tendency to alternation, but some special stress is required to make it evident, such as extrasystole or sometimes simple increase of the cardiac rate. In this group would be included, of course, the postextrasystolic or postpremature contraction alternation. In developed alternation the alternate larger and smaller pulse-waves are constantly present. It is generally assumed that the latent form, which is more frequent than the developed, shows a tendency to develop into the latter.

Simple methods are of little or no value in detecting postextrasystolic alternation, which can be done satisfactorily only by means of sphygmograms. Developed alternation can be discovered in many cases by palpation of the pulse, but the most satisfactory simple method is the use of the sphygmomanometer. It is at least as delicate a method as the sphygmograph when the alternation is continuous. The sphygmomanometer is connected with the patient as for taking the blood-pressure, and the pressure in the cuff raised to the maximum systolic pressure, as determined by auscultation over the brachial artery. At first only the alternate stronger waves come through and may be heard, then the alternate louder and weaker sounds are obtained usually through a zone of several millimeters of mercury pressure.

The sphygmomanometric method has been criticized on the ground that respiratory variations in pressure and pulsus bigeminus may be confused with alternation. The former may be ruled out by having the patient stop breathing or breathe in a very shallow manner for a few seconds while the test is repeated. The latter should have been detected previously by auscultation

of the heart in nearly all cases, if the examiner observes the rhythm carefully. Very rarely cases are encountered in which extrasystole occurs so late that coupling of the beats remains unrecognized. It is therefore wise, whenever possible, to repeat the study for alternation with an augmented cardiac rate. In this way not only is pulsus bigeminus easily detected and excluded, but alternation is increased, thereby confirming previously doubtful tests, or even a latent alternation may uncover itself.

It is sometimes stated that dicrotism may be mistaken for pulsus alternans. This gross error cannot occur if the examiner auscults the heart. Either alternation or dicrotism is immediately excluded.

**Mixed Arhythmias.**—The mixed arhythmias are rarely completely analyzed without graphic records. Nevertheless, the more conspicuous, which is usually but not always the more important, disturbance may frequently be recognized.

The principal complicating disturber of rhythm is the extrasystole. It may occur with practically any of the other types of abnormal rhythm. Since, excepting sinus arhythmia, extrasystoles are regarded as not evidencing so profound a cardiac disturbance as the other common arhythmias, their presence with one of the latter can hardly be considered of great moment unless they evidence a drug intoxication. Extrasystoles are probably found more frequently with auricular fibrillation than with any other of the arhythmias; their presence does not obscure the recognition of fibrillation, although the extrasystoles often remain undiscovered.

Occasionally, especially during convalescence from rheumatic fever, the combination of sinus arhythmia and slightly delayed conduction from auricle to ventricle is encountered. Here the latter is probably the more significant as evidence of cardiac damage, but the former would be the only one recognized without tracings.

Auricular flutter or auricular fibrillation in complete heart-block are interesting but rare forms of mixed arhythmia. The ventricular action and the pulse show the characteristic features

of block; without tracings the flutter or fibrillation could not be recognized.

I do not wish from this brief and incomplete survey to leave with you the impression that the clinical methods just discussed are absolutely conclusive in their results; it is seldom in clinical medicine that we are able to reach such a fortunate goal. The abnormal cardiac rhythms are notorious for the unusual manifestations they may exhibit; the literature of this topic alone would fill volumes. Furthermore, some patients are too ill to have carried out on them the various procedures that may be necessary to arrive at a diagnosis. But if we understand the mechanism of the abnormal rhythms and painstakingly dig out, with repeated examinations if necessary, the available clinical phenomena in each patient, keeping in mind the limitations of clinical methods, and where uncertainty still exists, favor the commoner condition, although graphic studies of the rhythm are a comfort to the physician and sometimes necessary for accurate diagnosis, it is seldom that any of our patients will suffer materially for lack of them.

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## CLINIC OF DR. TRUMAN G. SCHNABEL

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# GASTRIC DYSFUNCTION IN CASES OF INTERNAL SECRETORY DISTURBANCE

When the patients present themselves for treatment in this department they are hurriedly classified at the admission desk into four main diagnostic groups. Those with complaints suggesting gastro-intestinal disease are referred to this clinic. In many of these cases the original snap diagnosis assigning them to a gastro-intestinal category is justified by the subsequent study we are able to give them. In a certain number of cases a non-gastro-intestinal diagnosis is finally made, while in a third group the digestive tract is distinctly involved in addition to, or perhaps consequent upon, disease elsewhere in the body.

You have thus far been assigned in the main to the study of patients with symptoms pointing to the stomach and bowels and in whom these organs seemed to present the only abnormalities to be found. Today we propose to show 3 patients and give findings in 2 others in whom the presenting symptoms are either entirely or in part digestive, but in whom the real source of trouble is an extragastric one. It is generally recognized and emphasized that in disease no single system can be reckoned with apart from the remaining portions of the body. This being so, if you have not already seen such patients, you will have abundant opportunity to study pulmonary, metabolic, cardio-vascular, renal, and endocrine dysfunction cases in which the gastro-intestinal disturbances are a more or less prominent and often an annoying feature.

The disordered functionation of the so-called endocrine glands is rather striking in its effects. The pronounced types

are easily recognizable as one passes them on the street. In hyperthyroid cases much is made of the goiter, the eye signs or tachycardia, but little thought is given to abdominal discomfort after meals, "gas," nausea, or vomiting. In a small number of these cases the chief complaint is digestive, and only a careful general survey reveals some disordered function on the part of a gland of internal secretion. Frequently the clear-cut endocrinopathics are dismissed with the explanation that their indigestion is due to a "nervous reflex," when an intelligent understanding of their gastric dysfunction would point the way to helpful symptomatic relief. It must be noted, too, that many of the severe cases with internal secretory derangement are free of gastric symptomatology and that these may or may not reveal some changes in their gastro-intestinal motility, peristalsis, or secretion by test-meal or *x*-ray studies.

We shall not attempt a complete résumé of the cases we hope to present, but shall rather aim to call attention to findings and historic facts which will serve to illustrate the points we are trying to make.

The first case is probably one of Addison's disease. As you see her she appears deeply pigmented over her entire skin surface. This pigmentation is naturally more pronounced in the areas exposed to light, but the legs, feet, and trunk share in this happily styled "bronzing." The tongue and mucous membranes of the cheeks show grayish-black spots. From the beginning of her illness her chief complaints have been "great weakness" (general) with "stomach gas attacks and nausea." Up to the date of her first visit, one and a half years after the onset of her disease, nausea, regurgitation of food, and gas were very distressing, and were uniformly explained by her physicians as being due to "nerves."

Her blood-pressure now varies for the systolic reading from 80 to 100 mm., while the diastolic point reads from 55 to 75 mm. She complains at times of much numbness in the hands. An annoying symptom is that of cramp-like pains in the legs, especially in the left side, passing up to the lower back. She has a severe spot pain over the inner aspect of the left instep, usually

coming on at night. The blood Wassermann test and urine examination are negative. There is a mild secondary anemia with no unusual findings in the differential count. There are no evidences for an active inflammatory lesion in the lungs, and an *x*-ray of the chest only shows some increase in the linear markings and hilus shadows, with some few calcified glands. The von Pirquet reaction was markedly positive.

Fractional test-meals have never revealed the presence of free hydrochloric acid or of pepsin. The gastric contents have never shown occult blood and have always been gone from the stomach in one hour after an Ewald meal. Inflation of the colon was negative. There are no masses or palpable organs in the abdomen.

Dr. Pancoast found no gastric residue six hours after an opaque meal; the bismuth column had reached the transverse colon. The terminal ileum could be separated from the cecum. There was slightly more tenderness here than elsewhere in the neighborhood. After a second opaque meal the examination of the esophagus was negative. The stomach was long, low, and slightly sagging, with the greater curvature about 5 inches below the umbilicus. Peristalsis was very inactive, there being no well-defined waves. There was a constant hypermotility. No defects in the outline of the stomach were noted. There was no deformity of the duodenal cap. It was shown on subsequent examination that the entire colon is ptosed with a normal motility.

Just as soon as the achylia gastrica was discovered the use of dilute hydrochloric acid and pepsin served to end the gastric attacks and there resulted an increase in body weight. She has received an especially prepared extract of adrenal glands over a long period of time, apparently with no good effect. When the dose was increased to 9 grains of adrenal extract per day she vomited after each 3-grain dose. She is gradually growing weaker and the prognosis is, of course, bad. She is thus an endocrine patient whose remaining years have been made happier and perhaps somewhat prolonged by a proper appreciation of the nature of her gastric dysfunction.

This case has been presented in more detail than we had planned largely because Addison's disease is comparatively rare, and you may not see a similar case for some time to come. We have omitted many interesting features and diagnostic studies in her case, but one must be pointed out before we pass on to the next case.

If one, so to speak, draws with the finger-tip a square on the skin of the patient's abdomen, and waits for about a half minute, a pale line or band is noticed to appear in the track of the tracing finger. This white-lined square reaches its maximum clearness in one minute and persists for one, two, or even three minutes before being gradually obliterated. Care must be taken not to scratch the skin with the finger-nail or to press so hard that an immediate blanching occurs with perhaps some red lines in addition. The stroking must be done deliberately and can be done with the end of a fountain pen. The white lines eventually become wider than the actual area touched by the pen or finger.

This phenomenon is known as "the white adrenal line" and was first described by Emile Sergent, of Paris. It is therefore often styled the "Sergent white line." It is supposed to indicate hypoadrenia. Its author believes that in conditions in which arterial hypotension exists there is present a peripheral vasodilatation and that with light stimulation of the skin vasoconstriction replaces vasodilatation. In the French literature this "ligne blanche surrenale" is frequently mentioned. It seems to have little popularity in this country. If, however, it is a good indication of adrenal insufficiency, as many seem to think, we should often try it on our patients. There are undoubtedly other examples of hypoadrenia than that to be found in Addison's disease.

The next patient is an example of exophthalmic goiter or Graves' disease. This term suggests two of the findings in all similar cases. As you see, there is an exophthalmos or protrusion of the eyeballs with a tumor formation or enlargement of the thyroid gland. She seems apprenhensive, and such patients are styled by their friends as being "nervous." Their pulse-rate is

increased, especially so under circumstances such as she finds herself now. Some cases show various types of irregular action of the heart. There is in most patients a fine tremor of the outstretched hands with separated fingers. Their extremities are, for the most part, moist and cold. There are in these patients many evidences for vasomotor instability; for example, in this patient (Mrs. H) you see extensive transient erythematous patches on the neck and chest. Such an appearance should suggest an endocrine dysfunction. These patients all show a very marked epinephrin hypersensitiveness.

In order to determine the presence of this latter phenomenon patients should be put to bed at least a day previous to the test. All conditions must be arranged to make for complete composure on the part of the patient. Two or three control readings are taken at five-minute intervals of the blood-pressure, systolic and diastolic, the pulse and respiration rate. These readings should be fairly constant before the test is carried out. The subjective and objective condition of the patient should be carefully noted. Following this 0.5 c.c. of the fresh commercial 1 : 1000 "adrenalin chlorid" solution is deeply administered beneath the skin over the deltoid region. Readings of the blood-pressure, pulse, and respirations are made. In addition, any subjective or objective changes are noted. These observations and readings are made every two and a half minutes for the first ten minutes after the hypodermic; then every five minutes up to one hour, and then every ten minutes for a half an hour longer. At the end of one and a half hours the reaction has usually passed off.

In the so-called positive reactions there is an early rise in the systolic and a fall in the diastolic pressure readings. In mild cases the fall in the diastolic pressure may occur alone. There is a rise in the pulse-rate of at least 10 and sometimes as many as 50 per minute. In thirty to thirty-five minutes there is a moderate fall in the pulse and blood-pressure followed by a characteristic secondary rise and subsequent fall to normal. Briefly a clinical picture of Graves' disease is reproduced or exaggerated in this way. The adrenalin chlorid injection tried

by this method is popularly known as the Goetsch test, and seems to exhibit a patient's sensitiveness in proportion to the degree of hyperthyroidism present. The test is of diagnostic value in differentiating true hyperthyroidism from a very large group of clinical conditions which are borderline in nature. Of course, the well-defined cases need no differential tests for accurate classification. There are, however, many instances, particularly in patients exhibiting the familiar syndrome of fatigue, asthenia, loss of strength, loss of weight, nervousness in varying degrees, tachycardia, vasomotor instability and perhaps some elevation of temperature, in whom this test helps in making a more definitely positive or negative thyroid diagnosis. There are those, it must be noted, who have had little success with this test and, therefore, discredit its value.

In most of these hyperthyroid cases one finds, in addition to the things mentioned, the evidences of an increased liberation of energy. This energy is measurable in terms of body heat production. Under uniformly restful conditions normal individuals yield up about the same amount of calories per unit of body surface per unit of time. The physiologic chemist is able to determine for us what this amounts to by direct or indirect calorimetric methods. His results are expressed in the number of large calories per square meter of body surface per hour. Normally 40 C. is the amount of energy output of normal men with a 15 per cent. deviation being considered as decidedly abnormal. In hyperthyroid cases, as we have said before, there is a considerable increase of the basal metabolic rate. In a few instances this rate is not increased for hyperthyroid cases, but usually such patients will exhibit a positive epinephrin sensitiveness. Not all hypersensitive epinephrin patients fall into a Graves disease group, but a negative Goetsch test almost certainly rules out this possibility. The Goetsch test is easy of execution and requires little paraphernalia. The determination of basal metabolism is difficult for the untrained and requires a rather elaborate equipment and intelligent co-operation on the part of the patient. The basal metabolism rate falls with improvement in thyroid intoxication cases, and thus re-

peated estimations of this figure in any case serve as a splendid indication of success or failure in treatment.

The second case (Mrs. H.) falls very easily in the group we have just described. Her symptoms came on after the birth of her last child. She has a struma, tachycardia, mild exophthalmos, and all the evidences of a typical Basedow syndrome. These symptoms are now ameliorated after the practice of a modified rest cure carried out at home. She always has had and still has an enormous appetite, whose satisfaction was always followed by much gas, nausea, and post cibum discomfort. It was discovered by fractional test-meal extractions that her acid curve was rather high during the early stages of digestion, reaching 60 in forty-five minutes, and then gradually decreasing to low figures. A decinormal solution of sodium hydroxid is used in titrating the gastric contents for the acid values. No occult blood was found.

Dr. Pendergrass found the stomach to contain a slight residue six hours after a bismuth meal. The stomach was normal in position, size, and shape. After a second bismuth meal there was a slight pyloric spasm followed by slight hyperperistalsis and hypermotility.

While at rest in bed the diet for almost two weeks consisted almost solely of milk and cream given somewhat after the Sippey method. The feedings were administered every two hours, and each feeding was followed by the use of bismuth subcarbonate and magnesium oxid powders; of the latter, amounts were given sufficient to maintain a daily movement of the bowels. She had had some prior frequency in this respect. Lime-water was abundantly added to the milk-cream mixtures. Four times daily quinin hydrobromate, 0.3 gm., was prescribed. Occasionally sodium bromid was substituted. Besides this 0.1 gm. hypodermics of the cacodylate of sodium were given three times a week. Under this scheme with subsequent additions and alterations she has regained 8 of her 30 lost pounds. She is a typical case of hyperthyroidism with digestive symptoms relieved by measures calculated to reduce thyroid activity and counteract hyperacidity and a mild pylorospasm.

We will turn from this patient and present the studies made in 2 cases now in the hospital under Dr. Stengel's care. Under ward conditions the basal metabolism can be ascertained and here, too, the epinephrin injections may be tried. From an outpatient department it is difficult to have either of these tests properly carried out.

The first of these patients (Mrs. B.) has a basal metabolism of 98 per cent. above the normal. She does not now have, nor has she had, any digestive symptoms. Her stomach empties an Ewald meal in seventy-five minutes and the free acid figures reach the highest concentration in forty-five minutes when the titration reads 32. Her stomach showed no residue six hours after a bismuth meal and showed some hyperperistalsis and hypermotility after a second meal. The stomach was in good position and showed no other defects. This patient is apparently a rather marked case of exophthalmic goiter with no gastric symptoms and only slight evidence of motility and peristalsis dysfunction.

The second history is that of a woman (Mrs. C.) with a basal metabolism of 45.8 per cent. above normal. Her post Ewald meal curve shows a complete achlorhydria with the enzymes present. Dr. Pendergrass reports her stomach to be markedly ptosed, being well down in the pelvis. There was a considerable residue after a six-hour bismuth meal. After a second meal the peristalsis and motility were shown to be of an intensity usually seen in a stomach of the water-trap type. This patient in spite of her secretory faults and unusual gastroptosis is free of "indigestion" now. A number of years back she was the victim of severe abdominal attacks with constant post cibum nausea, fulness, and gas.

The third and last patient in this group is Mrs. P., who had a panhysterectomy performed ten years ago. Ever since this experience she has had much "stomach trouble" with nervousness. She has a ravenous appetite, but after-meal attacks of "indigestion" follow its satisfaction. She has other complaints which you will appreciate as being common in those who have lost the ovarian internal secretion, whether the loss is brought

about by excision of the ovaries or at the time of the physiologic menopause. She is a case of complete achylia gastrica on the strength of a single fractional gastric analysis.

Dr. Pendergrass found the stomach to contain no residue in six hours after a bismuth meal and it was of normal size and in good position. After a second meal the peristalsis showed exceedingly weak and infrequent, while the motility was subnormal. There was no deformity in the body of the stomach or in the duodenum.

She has been taking extract of ovarian tablets 0.13 gm. three times a day. In addition, she takes 2-c.c. doses of dilute hydrochloric acid with her meals. Her improvement has been quite surprising. She has no "indigestion" now after a month of such therapeutics. We have, however, failed to impress her intestinal stasis, which is quite evident on *x*-ray examination. We hope, however, that time may bring an improvement in this respect. This is one of the most difficult conditions we must deal with in our clinic.

A very natural question to put after seeing these cases interrogates as to the rôle played by the glands of internal secretion in normal or disordered action of the stomach or even in organic disease of this viscus. There are those who maintain that the wide-spread somatic influence of the endocrine system does not miss the gastro-intestinal tract. There is evidence for and against this viewpoint. Certain it is, that visceral function is largely under the control of the autonomic nervous mechanism and its component parts, the vagus and sympathetic systems. The thyroid and stomach receive fibers from both of these nerves. Some insist that thyroid secretion stimulates vagal tone and that the product of adrenal activity does the same for the sympathetic system. Some believe that thyroid secretion acts on both the vagus and sympathetic sides, and others think that thyroid sensitizes the sympathetic system to adrenal influence. On the other hand, it is likely that these theories hold no truth, but that the autonomic influence plays the primary rôle in endocrine dysfunction, and that its influence is exerted alike upon the gland and the hollow viscus concerned. There is, however, an

outstanding fact, difficult to gainsay, in the existence of gastrointestinal symptoms and dysfunction in many well-defined endocrine syndromes. Whether their relationship is one of effect and cause or merely of coincidence is not universally agreed upon.

Your attention has just been called to 2 cases in which there exists internal secretory disturbances and no gastric symptomatology with mild and rather extensive gastric dysfunction. You also have had an opportunity to see patients with internal secretory disturbances and very definite symptomatology with abnormal peristalsis, motility, and secretion on the part of the stomach. All of which would seem to point somewhat to coincidence as an explanation of "stomach trouble" in endocrine cases.

If stomach dysfunction is due to hyperthyroidism a natural consequence would seem to be a uniform behavior on the part of the stomach in Graves' disease. For example, one would always expect to find in exophthalmic goiter cases an overfunctionation of motility, peristalsis, or secretion. In hyperthyroid disease the gastric activity may be excessive, normal, or diminished. Some would explain this variable response by calling attention to a possible sequence of events in Basedow's disease. Often these cases begin with glandular hypersecretion and finally pass into a myxedematous picture. Corresponding, therefore, the gastric function may be excessive to begin with and eventually terminate in mild or extensive underactivity. The question of fatigue may be a big factor in these cases.

There is some evidence in the literature to show that adrenalectomized animals at autopsy have an increased number of gastric ulcers as compared with normal laboratory controls. This would seem to indicate the internal secretory origin of these lesions. Friedman believes that the first step in ulcer production is a neurosis induced by disturbed endocrine function. The neurosis is responsible for some circulatory changes in the gastric mucosa, and consequently some nutritional alteration with breaks in the surface continuity. Friedman does not deny the possible acid factor in ulcer development, nor does he deny the

possible central nervous system control exerted on the autonomic system.

We have found organotherapy of little help in gastric therapeusis. Perhaps our preparations were not sufficiently active. Results equally good may be secured by other and older methods. We have tried suprarenalin products in the overfunctioning conditions and thyroid preparations in the deficient conditions. Whatever the truth may be concerning endocrine and gastric dysfunction, we only wish to stress these points:

1. That gastric symptomatology in all patients regardless of type always indicates the investigation of gastric function if the patient is able to submit to test-meal and *x*-ray studies.

2. A knowledge of the nature of such gastric function points the way to intelligent therapeutics and probably some symptomatic relief.

3. Endocrine syndromes sometimes include gastric symptoms and gastric dysfunction.

4. The relationship of the glands of internal secretion and gastric functional disorders or even gastric ulcer is still a moot question. There may be such relationship.

## CLINIC OF DR. HENRY K. MOHLER

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### PERNICIOUS ANEMIA—GASTRO-INTESTINAL AND SPINAL CORD SYMPTOMS. REPORT OF A CASE

PERNICIOUS anemia is the term applied to a chronic disease for which no adequate cause can be assigned, and which is characterized by a progressively unfavorable course, with definite changes in the blood, the important ones being a great decrease in the number of red corpuscles with a relatively less reduction in the hemoglobin, as the result of which the color-index is high. The leukocytes are normal or slightly reduced in number.

The disease begins very insidiously in the majority of cases and the disorder usually has existed for some time before the patient regards himself as not being in a normal state of health. A very significant fact to be borne in mind in considering a patient as possibly having pernicious anemia is that usually there is very little loss of weight until in the last stages of the disease and that the subcutaneous tissues are well preserved.

Thomas Addison, in his monograph on the Constitutional and Local Effects of the Diseases of the Suprarenal Capsules, published in 1855, presented for the first time a clear and definite description of pernicious anemia, which he termed "idiopathic anemia," later called Addison's anemia. It was while he was studying the anemia associated with diseases of the suprarenal capsules that he discovered a type of anemia which was a clear and distinct clinical entity and differed greatly from the severe secondary anemias including those due to disease of the suprarenal capsules, now commonly known as Addison's disease. Pernicious anemia has been the subject of many investigations conducted by numerous clinicians and laboratory workers since

Addison's Monograph, and a number of causes have been assigned for its occurrence, all of which have failed to fully meet the requirements of being the etiologic factor of the disease.

As in a number of other diseases, sooner or later probably some observer will definitely show that the blood changes in pernicious anemia are but the effects of a poison acting upon the tissues of the body, and that there is no more reason for terming pernicious anemia a primary anemia than it would be to call the anemia due to the toxins of intestinal parasites a primary anemia.

It has been stated that the following facts suggest that the poison which causes the destruction of the red corpuscles exerts its effect on other organs simultaneously because in some cases the spinal cord shows evidence of the disease earlier and more advanced than the blood changes, and that the fatty changes of the heart, liver, and kidneys are not to be explained as the result of the anemia. It is much more likely that the anemia, the spinal cord lesions, and the fatty changes are co-ordinate manifestations of the same unknown poison. Another reason for believing that the symptoms are not the result of the anemia is that the weakness, dyspnea, etc., do not always get better as the blood improves, or worse as the blood deteriorates.

The diagnosis of pernicious anemia may be strongly suggested, but usually it is the symptoms considered in connection with the complete blood count that finally establishes its identity.

As blood counts are becoming more frequent in the routine examination of patients, so today we are seeing diagnosed more frequently cases of pernicious anemia. There is no reason to believe that there is an increase in the frequency of the occurrence of the disease, but rather an increased recognition of the disorder as the result of the increased number of blood examinations made. Pernicious anemia is distinctly a disease of adult life and before the age of thirty-five years is slightly more common in women than in men, and after thirty-five years it is twice as common in men as in women.

Some of the diseased conditions which present symptoms common to those present in pernicious anemia have been considered as causative factors of pernicious anemia.

Among the conditions so considered are pregnancy, the puerperal period, syphilis, repeated losses of blood, as in hemorrhoids and in menorrhagia. Intestinal parasites are the cause of an intense anemia, but such cases are not included under pernicious anemia because of its established etiology. Diseases of the gastro-intestinal tract including gastric and intestinal sepsis, chronic diarrhea, carious teeth, abscessed roots of the teeth and pyorrhea have been considered by some observers as etiologic factors in producing pernicious anemia. A certain number of patients attribute their illness to severe mental or nervous strains and prolonged intense depressing emotions.

In the diseases and conditions named as factors in causing pernicious anemia no exponent of any one disease or group of diseases has fully shown that pernicious anemia is the outcome thereof.

The findings at autopsy in cases of pernicious anemia suggest that the changes in the body tissues are principally found in the blood, spinal cord, the long bones, the heart, the liver, and the kidneys. The fatty portions of the bone-marrow are replaced by red, active, blood-making tissues. Deposits of iron pigment are present in the liver, spleen, and lymph-nodes. The skeletal muscles are bright red in color in contrast to the striking yellow and usually well-preserved layer of fat, with small hemorrhages scattered throughout the tissues.

Lesions of the spinal cord in Cabot's series of 82 autopsies were present in 84 per cent. of the cases. The lesions, degenerative in character, were most pronounced in the cervical region of the cord and most often located in the posterior columns. In addition to these findings patches of sclerosis are often found scattered in the lateral columns for a considerable distance along the cervical and dorsal region of the spinal cord.

The early symptoms of this disease in almost every instance are very similar and remain so for a variable period. The onset of the disease is slow, not attracting very much attention, so that the patient may be unable to definitely say just when he thinks the languor and weakness began, which gradually became more and more evident.

The first symptom most common to all patients is general weakness. There is an increasing lack of desire to make effort because of the sense of feeling faint or a sense of breathlessness on attempting any physical effort or displaying any emotion. Palpitation of the heart is readily induced in almost every attempt to do anything requiring even ordinary effort.

Next to the sensation of weakness and languor probably the most common group of symptoms complained of are those referable to the gastro-intestinal tract. This group of symptoms, though generally accompanying the weakness and languor, occasionally precedes the latter.

After the gastro-intestinal symptoms, the nervous system furnishes the origin of the most numerous complaints. General weakness may be accompanied by vertigo, headaches, and blurred vision.

In not a few patients the mental symptoms, such as inability to concentrate, low spirits, irritability, appear early in the course of the disease; and in addition to the general asthenia are more or less a constant feature throughout the entire course of the disease.

The entire surface of the body early in the disease presents a pallor with a waxy appearance and the mucous membranes are blanched. Even in the presence of the already described symptoms and general appearance the body weight is well preserved and emaciation is a late symptom if present at all, due to the result of malnutrition from severe gastro-intestinal disturbance.

Gradually the signs and symptoms of anemia become more marked and the skin of the patient is often thought to be jaundiced in contrast to pearly white appearance of the sclera of the eyes. As a matter of fact jaundice is rarely present and the so-called jaundice is the lemon-colored tint imparted to the skin which is so characteristic and diagnostic of pernicious anemia.

The symptoms may well be considered under two headings: first, those symptoms due to the anemia; second, those symptoms that are more or less peculiar to pernicious anemia and not necessarily present because of the anemic condition of the blood. Loss

of strength, shortness of breath, palpitation, headache, vertigo, edema are symptoms that may be present and be due in their entirety to secondary anemia.

Among the symptoms peculiar to pernicious anemia are those referable to the gastro-intestinal tract. These symptoms vary greatly in character and degree, and may be so slight as to be termed mild attacks of indigestion or of so severe a gastro-intestinal disorder that they simulate ulcer or carcinoma of the stomach. It is not uncommon to have as early symptoms abdominal pains, with or without diarrhea, and usually bearing no relation to the taking of food or the character of the food.

The absence or greatly diminished amount of hydrochloric acid is found upon the chemical examination of the stomach contents. This condition, known as achylia, is present in practically every case of pernicious anemia, and the gastric symptoms do not seem to bear any relation to the degree to which the hydrochloric acid is reduced. The achylia has been explained as being the result of the atrophy of the gastric mucosa which is present so commonly at autopsy in cases of pernicious anemia.

The attacks of indigestion are not continuous, but at times for considerable periods there is an entire absence of symptoms referable to the gastro-intestinal tract.

No satisfactory explanation has been offered for the occurrence of the gastro-intestinal symptoms, and no treatment is effective for the relief of these symptoms. For no apparent reason the gastro-intestinal symptoms appear and for the same reason subside, leaving the patient in an exhausted condition. Stomatitis is also encountered during the course of the disease.

Another prominent group of symptoms present in pernicious anemia are those referable to the spinal cord. This group is not only important, but present in many more instances than generally recognized. If these symptoms are looked for they are generally found to be present in cases of pernicious anemia and are important in helping to establish a diagnosis of this disease.

The spinal cord symptoms are present in varying degrees, and in one group of patients the spinal cord symptoms are the earliest and more prominent than those due to the anemia, a second

group of patients in which spinal cord symptoms are slight and always overshadowed by anemia, and a third group in which no obvious symptoms referable to the spinal cord were noted, yet autopsy revealed definite lesions in the spinal cord.

Practically every patient shows to some degree numbness, tingling, and other abnormal sensations in the extremities, even in the absence of changes in the spinal cord at autopsy. Paresthesia is an occasional symptom.

As a result of the more or less extensive changes in the cord the cases presenting spinal cord symptoms may be grouped, first, as those with symptoms of a spastic gait, increased reflexes, and some degree of paralysis, and second, those cases in which the symptoms are suggestive of locomotor ataxia. In most of the patients presenting symptoms of spasticity, sooner or later, the patient complains of incontinence of the urine and feces, with areas of anesthesia in the lower extremities.

Just as in cerebrospinal syphilis, so may we find in pernicious anemia many types of disorder of the motor or the sensory function of the cord, as unsteady gait, lightning pains, girdle sensations, hyperesthesia, and severe neuralgic pain.

Among the mental symptoms that have been noted in pernicious anemia may be mentioned mania, depression of the melancholic type, dementia, delirium, and antemortem coma is not uncommon, and may be present for a period varying from several hours to several days before death occurs.

The skin, in addition to being blanched early in the course of the disease, subsequently to become a lemon-yellow tint, may rarely be pigmented as in Addison's disease of the suprarenal gland, or patches of vitiligo may be present.

The patient who comes before you today came under our observation six months ago, and from our studies we concluded that the case was one of pernicious anemia. He presented symptoms referable to the gastro-intestinal tract early in the history of the course of his illness which began October, 1917, and now the symptoms are prominently those referable to the spinal cord, with no complaint of gastro-intestinal disorder.

The following is the clinical record:

C. M. L. Male, age forty-five years, American born, married, occupation insurance agent, except for a period during which he served as a soldier in the Spanish-American War.

**Family History.**—Father dead, cause unknown, aged seventy-five years when he died. Mother living and well, age sixty-eight years. Four brothers living and well.

**Personal History.**—Patient had measles, mumps, chicken-pox, and whooping-cough during childhood. Prior to the present trouble always enjoyed good health in spite of the fact that he was never very robust. Served in the United States Army as a soldier in the Spanish-American War and enjoyed good health during his career in the army, but for an attack of dysentery for which he was given ambulatory treatment over a period of three or four months before he finally became symptom free. He never used alcoholic drinks and has not suffered from malaria, metallic poisonings, or venereal infections.

**Present Trouble.**—In October, 1917 patient noticed for the first time that his strength was failing him, and almost simultaneously, as he remembers, he began having "stomach trouble" for which he could in no way account. His friends called his attention to his pallor and his weight was 5 pounds less than one year previously, the last time he had been w ighed. He attributed his loss in weight to the attacks of indigestion and vomiting. After having consulted a number of physicians he was finally told by a surgeon, to which he had been referred, that he had a tumor in the stomach. The surgeon told his wife that the tumor was cancer of the stomach and advised an operation. The operation was performed, no cancer was found in the abdomen, and the only abnormal finding was a thickened gall-bladder, which was drained.

The patient remained in the hospital for five months and convalesced very slowly for a period of about one year, at the end of which time he felt very much improved, having regained his strength. Since his operation he has had no gastro-intestinal symptoms. The color of his skin was not improved, and he states he was frequently told of the yellow color of his skin. His weight increased 5 pounds, so that he weighed the same as he

did in 1916, one year before his illness. His general condition was very much improved, although his strength was never as great as it was before he was taken ill. About one year ago he noticed "trouble in walking" because of the weakness and numbness in his lower extremities. He states that his legs would not respond to his efforts to move them as they had done previously. The numbness extended from the toes to the waist-line. There was no loss of control of the sphincter of the bladder or bowels.

**Physical Examination.**—Patient is moderately well nourished, no evidence of emaciation.

*Eyes.*—Pupils equal, react normally to light and accommodation. Sclera not jaundiced.

*Mouth.*—Tongue pale, clean, and moist.

*Teeth.*—In good condition, small superficial amalgam filling in lower left molar; no pyorrhea.

*Tonsils.*—Negative.

*Chest.*—Expansion shallow, but equal.

*Lungs.*—Clear and resonant throughout; no râles are heard.

*Heart.*—Cardiac dulness, normal in outline. Muscular tone of first sound of heart at the apex poor; sounds are distant. An inconstant soft systolic murmur is present at the apex.

*Abdomen.*—Operation scar in epigastrium. No masses or areas of tenderness palpable. Liver, spleen, and kidneys not palpable.

*Extremities.*—No tenderness. No edema. Knee-jerks greatly increased, ankle-clonus and Babiniski present, no Rhomberg present.

*Skin.*—Upon the exposed surfaces of the body the skin has a light bronze appearance, in contrast to the skin on the covered parts of the body, which is of a yellow waxy color. No loss in sensation.

*Rectal Examination.*—Negative.

**Laboratory Examination.**—Twenty-four-hour specimen of urine: Quantity 1100 c.c.; specific gravity 1.020, and a very faint trace of albumin, with few hyaline casts, otherwise the urine was negative.

*Wassermann test* of blood and spinal fluid is negative.

*Feces* show no blood, ova, parasites, mucus, or pus.

*Blood Count.*—Red blood cells, 2,070,000; white blood-cells, 6000; hemoglobin, 50 per cent; color index, 1.2 plus.

*Differential Leukocytes.*—Polynuclear, 60 per cent.; small lymphocytes, 34 per cent.; large lymphocytes, 5 per cent.; eosinophils, 1 per cent.

*Gastric Analysis* (Fractional Test).—Test meal: 2 pieces dry toast, 500 c.c. water given 7.30 A. M. Residue in stomach 50 c.c. before giving test meal.

| | Minutes | | | | | |
|---|---|---|---|---|---|---|
| | 15 | 30 | 45 | 60 | 90 | 120 |
| Free acid | 0 | 0 | 0 | 4 | 4 | 3 |
| Total acid | 5 | 8 | 10 | 12 | 12 | 10 |
| Lactic acid | + | + | + | + | + | + |
| Blood | — | — | — | — | — | — |

Examination of spinal fluid is negative for increased cells and globulin.

The patient presents a number of interesting points in his history worthy of discussion.

Did the patient at the time of his gall-bladder operation have the blood condition from which he is now suffering? It must be remembered that while the gall-bladder was drained, the operation was performed on the strength of a diagnosis of carcinoma of the stomach made on *x*-ray examination, chemical examination of the stomach contents, and the gastro-intestinal symptoms. These symptoms were nausea, vomiting, and actual paroxysms of pain in the epigastrium, for which no reason could be assigned and which pain was in no way related to the taking of food. The findings common to both pernicious anemia and carcinoma of the stomach are the low acidity, with the presence of lactic acid in the chemical examination of the test meal, the nausea, the vomiting and paroxysms of pain in the epigastrium, with the loss of strength, pallor, and a confusing *x*-ray picture. Cabot states that in the case of pernicious anemia an *x*-ray examination had been incorrectly diagnosed carcinoma of the stomach.

The gastric analysis of the patient under consideration made

six months ago is quite in keeping with the findings of carcinoma of the stomach, and although no record of the gastric analysis made prior to the operation three years ago is obtainable, it is safe to assume that a marked subacidity was present then as it is at the present time, in view of the diagnosis of carcinoma of the stomach having been made. The patient is now free from gastro-intestinal symptoms and has been since the operation. The achylia which is now present is, therefore, not causing any symptoms referable to the stomach.

It is most unfortunate that no blood examination other than a Wassermann was made prior to the operation. When the patient was seen six months ago it was only after a blood count had been made that the identity of the disease was definitely established, although the appearance of the patient with the history and the presence of symptoms referable to spinal cord suggested pernicious anemia.

In view of what we now know we are warranted in assuming that pernicious anemia existed at the time of the operation.

Why should the operation of simple drainage of the gall-bladder relieve the patient of his gastro-intestinal symptoms?

Two reasons may account for the disappearance of gastro-intestinal symptoms:

First: In the average case of pernicious anemia with stomach symptoms probably during one-half of the time the patient is free from gastro-intestinal symptoms. This group of symptoms appears and disappears without any apparent cause, and regardless of any type of treatment instituted.

Second: One of the best forms of treatment for any patient suffering from pernicious anemia is rest in bed, and the patient spent five months almost continuously at rest in bed following the operation. This period of rest may have been instrumental in bringing about a remission in the course of the disease of a two-year period, or until the beginning of the symptoms referable to the spinal cord which began one year ago.

During this patient's illness at no time has he suffered from diarrhea. There is, however, a history of having had dysentery for a period of four months during the Spanish-American War.

In some cases of pernicious anemia a history of diarrhea of long standing either preceded or accompanied the early symptoms of pernicious anemia, but it is not likely that a period of twenty years would elapse in which normal health was enjoyed before any symptoms would develop indicating a relationship between the dysentery and the pernicious anemia.

The dysentery, although the patient does not definitely recall, was probably dietetic or bacillary rather than parasitic in type, because of the ambulatory form of treatment as well as the frequency of these types of dysentery at that time. During the course of pernicious anemia there are frequently periods of remission during which the symptoms are absent or very slight and the patient's condition stationary or improved. It is the exception for a remission to last for a greater length of time than a period of from two to three years. The average duration of a remission is less than one year.

The history of the course of the illness of the patient under consideration suggests that he passed through a remission of two years following the operation, lasting until the appearance of the present symptom, viz., namely, "difficulty in walking."

This difficulty in walking is described by the patient as being due to lack of strength in the legs to move the extremities, hence the dragging of the lower extremities. On physical examination the knee-jerks are greatly exaggerated, with ankle-clonus and Babinski and some spasticity. We are evidently dealing with changes in the spinal cord producing the spastic type of changes in the extremities in pernicious anemia. Incontinence of urine and feces commonly associated with this type are absent in this patient.

The numbness and tingling sensations complained of by this patient which are confined to the region extending from the waist-line to the toes are symptoms complained of by patients afflicted with this disease. These sensations may be felt in various regions of the body or may be present over the entire body. We cannot always ascribe the symptoms of tingling and numbness to spinal cord changes, since in a number of instances autopsy revealed no gross or microscopic changes in the spinal cord.

The skin in almost all patients, as in this patient, suffering with pernicious anemia shows as an early change a pallor with a waxy appearance, later the pallor is replaced by a lemon-colored tint which may be incorrectly diagnosed jaundice. Our patient under consideration presents upon the exposed surfaces of the body a light bronze color which somewhat resembles a true sunburn and upon the unexposed surface of the body the skin is of a distinctly lemon-color tint. The patient has been aware of the bronze color of the skin for the past year and believes it was contracted while he was taking sun-baths in the southern part of the United States. A brownish pigmentation of the skin has been described in pernicious anemia patients induced by prolonged use of arsenic or large doses of this drug. In this case no arsenic was taken and therefore does not account for the bronze discoloration of the skin.

In pernicious anemia there is excessive amounts of blood destruction and the blood pigment containing iron is capable of being deposited in the skin. A more likely explanation of the bronzing of the skin on the exposed surfaces of the body is that the rays of the sun during the sun-baths in some way acted upon the iron pigment in the skin on the exposed surfaces of the body, so that the color was changed in contrast to that of the unexposed part of the body causing this bronze discoloration.

No areas of leukoderma or vitiligo are present as has been reported among the skin changes observed in patients suffering from pernicious anemia.

The mucous membranes shows no areas of pigmentation.

The diagnosis of this interesting case was made upon the laboratory tests. The examination of the stools was negative, thereby excluding chronic hemorrhage and parasites as the cause of the anemia. Syphilis was excluded as an etiologic factor by the finding of a negative Wassermann in the spinal fluid and the blood.

The examination of the spinal fluid shows a sterile fluid with no increase in cell content or globulin, thereby eliminating an infection of the spinal cord or its membranes.

The main features in the blood count and examination of the

stained film of blood of the patient were a great reduction in the number of red blood-cells, being 2,070,000, with a hemoglobin reading of 50 per cent. You will note that while the red blood-cell count and hemogloblin are reduced, the reduction in the hemoglobin is proportionately less than the reduction in the number of red cells, hence it follows that the individual corpuscle has a greater amount of hemoglobin than ordinarily found in health, a color-index greater than 1.

A blood count showing an anemia with a color-index of 1 or greater than 1 is almost pathognomonic of pernicious anemia, especially with a normal or slightly subnormal leukocyte count.

The leukocyte count in this patient is 6000 per c.mm, Microscopic examination of a stained film shows notable changes in the red blood-cells, principal of which are the increased size of many of the cells and the presence of nucleated red blood-cells. Many of the red cells are no longer circular in outline, but are pear shaped. This change in shape is known as poikilocytosis, and the increased size of cells is known as megalocytosis, both conditions which may be present in severe secondary anemias, but usually not to the extent that they are present in pernicious anemia. The megalocytosis accounts for the increased amount of hemoglobin and the high color-index of the red blood-cell.

The general weakness in the patient can readily be ascribed to the reduction in the number of red blood-cells, but it is remarkable that patients have been able to continue at work, and after reporting to a physician because of illness a blood count showed that their red blood-cells had been reduced to the neighborhood of 1,000,000 per c.mm. and were found for the first time to be suffering from pernicious anemia.

This observation shows that there is no constant relation between the reduction in the blood count and the severity of the symptoms.

Another observation that has been made is that with general improvement in the condition of the patient the color-index, which is high, may return to normal, with a reduction in size of red blood-cells as well as the disappearance of nucleated red blood-cells.

These changes have been observed during a period of remission. During the past six months the six blood counts which have been made show so little change from the original that we can practically consider the blood condition unchanged. Four nucleated red blood-cells to 100 leukocytes was the average found in the several blood examinations, with many megalocytes in all blood examinations.

No count has been made of the blood-platelets, but they are usually low in pernicious anemia.

The leukocyte count, which was 6000 per c.mm., shows 60 per cent. polynuclears, 34 per cent. small mononuclears. These percentages are within the range of normal. The common findings in the percentages of leukocytes in the blood count of pernicious anemia is a relative increase in the percentage of lymphocytes at the expense of the polynuclear cells. No myelocytes, which at times is a common finding, were found present in any of the seven blood examinations made.

The review of this patient's history can but emphasize the importance and necessity of making blood counts on all patients, especially those whose condition warrants surgical interference or who have a chronic impairment of health.

In establishing the diagnosis of pernicious anemia it is important to exclude the anemias of known origin classed as secondary anemias in contradistinction to pernicious anemia, which because of its unknown origin is termed a primary anemia.

A severe secondary anemia due to parasites, hemorrhage, and malignant conditions may resemble pernicious anemia, but one or more examinations of the blood will show that the color-index is low, less than 1, the red cells not of the megalocytic variety.

The history of a pernicious anemia patient does not record any hemorrhage as part of the disease unless they be petechial or retinal, in which the loss of blood need not be taken into account. Hemorrhages of considerable size are uncommon. No examination of the fundus of the eyes of our patient under consideration was made, since no symptoms referable to the eyes were complained of.

**Prognosis.**—The disease is almost without exception fatal

in periods varying from three to four years, although some patients have a history of having had the disease ten to fifteen years and few succumb to the disease in less than one year. It is safe to say that a patient whose blood is nearly normal and who has been free of symptoms for a period of six years will not have a recurrence.

**Treatment.**—In the absence of a known cause our efforts must be directed toward the treatment of symptoms. Rest in bed gives the patient the greatest relief from symptoms, especially early in the disease. Good, nourishing food, an abundance of fresh air and sunshine, and an equitable temperate climate will provide the patient with the greatest comfort. The food should be chosen so that it will cause no interference with appetite or diarrhea. Elimination must be kept at its best.

Arsenic in some form to increase the number of red corpuscles is the best drug we possess.

Blood transfusion is a very valuable aid in treatment and is productive of good results, however, usually only temporary, but the effects thereof may be the beginning of a period of remission. The blood transfusion should be so frequent as to keep the red cell count as near normal as possible. It may be necessary to transfuse every week to accomplish this end. Either citrated blood or transfusion by the direct method may be employed, the latter method being preferred.

## ADDISON'S DISEASE—DISCUSSION OF SYMPTOMS. REPORT OF A CASE WITH AUTOPSY FINDINGS

THOMAS ADDISON in 1849, while conducting his studies on patients with pernicious anemia observed that there was a group of patients with symptoms very similar in many respects to those of pernicious anemia, with evidence of destructive lesions of the suprarenals found at autopsy. In Addison's monograph "On the Constitutional and Local Effects of the Diseases of the Suprarenal Capsules" published in 1855 was described the syndrome which we now term Addison's disease. He described it as an iodiopathic anemia, associated with disease of the suprarenal glands and characterized by bronzing of the skin, disorders of the gastro-intestinal tract, and disturbances of the nervous system leading to a chronic cachexia and terminating fatally.

The suprarenal gland consists of two distinct parts, the medulla or inner portion of the gland and the cortex or the outer portion of the gland. The origin and function of these respective parts are also different. The cortex is derived from the germ epithelium and the medulla is an integral part of the sympathetic system, to which source it also owes its genesis.

The cells of the medulla show a special affinity for the chromium compounds and hence have been called chromophil cells. It is believed that the cells having this affinity for the chromium salts are but part of a system which is widely distributed throughout the body and closely resembles cells found in the sympathetic system in the carotid body and along the aorta.

The medulla contains in addition to these chromophil cells a plexus of veins. The chromophil cells of the medulla and other portions of the chromophil system produce and supply to the blood-stream the important substance called epinephrin. When the suprarenal glands are removed from higher animals the animal dies. Investigation shows that death is due to loss of the cortical part of the gland rather than to the medulla. Important

as the structure is, there are a sufficient number of chromophil cells outside of the suprarenal gland to sustain life, but no tissue can make up for the loss of the cortical cells. The cells in the cortex are arranged differently from the cells of the medulla, and are loaded with a peculiar fatty substance and contain brown pigment granules.

The only active principle of the suprarenal gland so far known is epinephrin, a substance which raises blood-pressure.

Many different functions have been assigned to the suprarenal gland by various investigators, among which are chiefly the following: to assist in maintaining a constant state of tonus in smooth muscle; to neutralize poisonous products of metabolism (detoxicating function); to regulate the metabolic rate in an emergency when other parts of the chromaffin system are unable to supply epinephrin in proper amounts.

The great advance made in our knowledge of ductless glands in general has stimulated a corresponding increase in interest and research in Addison's disease. Little has been added to our knowledge of the clinical features since Addison's original description, except the information that naturally would result from the study of a constantly increasing number of patients.

A more intimate knowledge of the suprarenal products may help us in the future to a better understanding of Addison's syndrome. At the present time we must be content to consider it as a result of disease of the suprarenal gland and characterized by muscular and vascular asthenia, bronze or brown pigmentation of the skin, increasing loss of strength, with a tendency to gastro-intestinal disturbances, and invariably a fatal outcome.

It has been pointed out by Weisel that disease of the medulla alone is not sufficient to account for this syndrome, but that a lesion involving the cortical cells is necessary to produce the grave symptoms. Likewise lesions of the chromaffin system located outside the suprarenal gland can produce part of the syndrome. A constant weakness of the sympathetic nervous system itself is capable of producing the pigmentation in Addison's disease. Since the chromaffin system is under the influence of the splanchnic nerves and the solar plexus, the primary lesion

responsible for the syndrome may be in the sympathetic nervous system.

Addison, in a discussion before the Royal Medical and Chirurgical Society, called attention to the close anatomic relation of the sympathetic ganglia, solar plexus and the suprarenal glands, and emphasized the correlation between disease of the two systems and the effect that such disease might have on general body health. The symptoms which such diseases produce are what has since become known as Addison's disease.

It is not uncommon in cases of Addison's disease to have an anatomic and functional inferiority present from birth. This underdevelopment is observed in connection with the condition known as status thymicolymphaticus, which is believed is due to suprarenal insufficiency resulting in failure of the involution of the thymus, hyperplasia of the lymphatic tissues, and hypoplasia of the circulatory and genital system.

Pathologic changes were noted in the suprarenal glands in 88 per cent. of cases of Addison's disease analyzed by Lewin. Pigmentation was absent in 28 per cent. of the cases of adrenal disease. The lesion most commonly found is tuberculosis. It may involve one or both glands. The tuberculous process is very rarely primary in the suprarenal capsule, but far more commonly is a part of a general invasion of the body by tubercle bacilli. Next to tuberculosis of the gland, atrophy is found to be present most frequently.

Simple atrophy or the atrophy resulting from chronic interstitial inflammation with contraction and compression of the medullary portion occurs. The glands may be so markedly atrophied that at autopsy they may be found only with difficulty.

Addison's disease is not of common occurrence. It is more frequently present in men than in women, and between the age of twenty and forty years. The onset of the disease is usually slow and characterized by a gradually increasing muscular weakness, with a pronounced disinclination to make any physical or mental effort.

Early in the illness gastro-intestinal symptoms may become a prominent feature. In some instances, however, symptoms

referable to the digestive tract are absent. When present they consist of nausea, vomiting, gaseous eructation, heartburn, epigastric or abdominal tenderness in varying degree. The bowels may be very irregular. One or more of the symptoms may be present, and the symptoms vary from time to time in kind, duration, and degree.

When diarrhea is present the weakness is usually very much increased. In the latter stage of the disease the nausea and vomiting greatly increase the existing weakness because of the effort required and because of the resulting lack of nourishment. When there is an absence of gastro-intestinal disorder it may occasionally happen that the patient has an enormous appetite. This is more likely to occur early in the disease, and polydipsia and polyphagia may be associated symptoms.

The general weakness complained of is a very prominent symptom and bears very much the same importance in this disease as it does in the symptoms of pernicious anemia. The muscular weakness is not necessarily accompanied by wasting of the body tissues. The general loss of strength early in the disease does not, however, require the patient to become bed-ridden, and it is not uncommon for patients during the course of the disease, after having been confined to bed, to become stronger temporarily and be about again for a varying period of time.

Recently a male patient in a convalescent home suffering with Addison's disease came under the observation of the writer having been sent from the medical service of a hospital, where apparently he had become greatly improved. After five days in the convalescent home the patient was returned to the hospital because of weakness and gastro-intestinal disturbances, and within a period of one month the patient died. This patient was evidently in the latter stage of the disease, but the improvement was so marked for a period that it seemed desirable to discharge him from the hospital to the home for convalescent care.

Pigmentation usually occurs early in the course of the disease, and occasionally it is recognized as the first symptom, but the time of occurrence, the distribution, and extent are extremely variable factors.

The pigmentation also varies in color, usually a difference in the degree of intensity from a light brown or bronze to deeper shades of brown, even at times a smoky black. The skin is pigmented to a greater degree in the normal areas of pigmentation, such as the areola about the nipples, in the groins, axilla, and about the genitalia. It is not uncommon for areas of vitiligo to develop and stand out in marked contrast in the areas of pigmentation. Pigmentation of the mucous membranes is present in the majority of cases. As a general rule pigmentation begins on the face, neck, and upper extremities. The mucous membranes of the lips along their line of contact may show a dark line of pigmentation, and areas of pigmentation may develop in the mucous membrane of the mouth, on the tongue, or a brown line may extend near the margin of the gums. It is not common for the scalp to show areas of pigmentation, although the hair may become darker or change color during the course of the disease. The nails show different degrees of pigmentation. The areas of the body exposed to the weather are frequently pigmented to a greater degree than the unexposed surfaces of the body.

The complete syndrome of Addison's disease without pigmentation has been described, and a lesion of the suprarenal glands found at autopsy.

Sergent describes a white line as an evidence of suprarenal insufficiency. It is produced when a blunt instrument is drawn firmly across the skin, after which is observed a broad white mark slowly appearing, remaining several minutes, and gradually disappearing. It is the result probably of some vasomotor disturbance.

The earliest nervous symptoms noticed are mental apathy, associated with depression and usually insomnia, although later the insomnia may be displaced by periods of drowsiness. Vertigo and syncopal attacks are not uncommon and are often brought on by effort, and, no doubt, result from great weakness.

The patient may attempt to make a greater effort than his strength will permit, with the result that syncope occurs, associated with sweating and a cold and clammy skin.

Severe neuralgic pains throughout the body are a not uncommon complaint.

The circulatory system shares in the general asthenia. The myocardium lacks the strength necessary to produce a forcible heart-beat and the pulse volume and blood-pressure are subnormal.

The blood itself, although the disease was thought by Addison to be an anemia, in most cases remains unchanged, and even late in the disease may be but slightly altered from the normal. At times the blood count may be high, due to concentration to body fluids as the result of vomiting or diarrhea. Fever during the course is uncommon, unless due to complications and a subnormal temperature is usually the rule. The skin often gives the impression to the touch that the patient has a subnormal temperature, which when taken by mouth verifies the observation. The skin is, as a rule, smooth and elastic, these symptoms being important in the differential diagnosis of other skin conditions with pigmentation, many of which are rough and scaly.

The diagnosis of Addison's disease is not easy unless all the cardinal symptoms are present. A history of general weakness, gastro-intestinal disturbance, pigmentation of the skin and mucous membranes, with no disease of the viscera or blood, are evidences which warrant a diagnosis of Addison's disease.

The cases which present the greatest difficulty are those in which pigmentation alone is present and in which the other symptoms are much delayed or not very marked. Pigmentation alone cannot be considered sufficient evidence to justify a diagnosis of Addison's disease. Other causes of pigmentation must be carefully taken into consideration and differentiated from Addison's disease, such as Graves' disease, bronze diabetes, pernicious anemia, cachexia accompanying malaria, syphilis, malignancy and tuberculosis, chronic skin disorders, vagabond's disease, chronic eczema in pellagra, arsenical pigmentation and pigmentation seen in chronic gastro-intestinal disorders, and long-continued chronic irritations of the skin.

The following is the history of the patient: Mrs. E. C.,

white, aged thirty-eight years, who was admitted to the hospital August 6, 1920, and died August 18, 1920.

**Chief complaint** on admission was general weakness.

**Family History.**—Father living and well at age of seventy-six years; mother living and well at age of fifty-six years; 4 brothers and 2 sisters living and well; 1 brother and 1 sister died of diphtheria. No history of cardiac, renal, or malignant disease in the family.

**Personal History.**—Patient had measles and chicken-pox during childhood; general health has always been the very best until the present illness. Menstruation established at thirteen years, was always regular until it disappeared four months ago. In 1906 patient was married and now has a boy thirteen years of age. Patient has had no miscarriages. Habits have always been excellent. Appetite good, bowels constipated. Patient does not recall having any injuries or operations

**History of Present Illness.**—Began in June, 1919, when patient, who had been in good health, was taken ill with an acute colicky pain throughout the abdomen, accompanied by vomiting. There was no fever, no tenderness. Forty-eight hours after the attack began patient became jaundiced, free from pain, but the nausea and, at times, the vomiting persisted. Immediately following the onset of the disease the patient was taken to a hospital for treatment and was told by the physician that she had "liver trouble." She felt at the end of two weeks that she was not benefited by her stay in the hospital, and she decided that she would return to her home and place herself under the care of her family physician. She was kept in bed at home continuously for eight weeks and during that time her weakness remained about the same. Against the advice of her physician she got up and about for several hours each day. Patient states that she had been constantly losing strength and her loss in weight during the past year has been 30 pounds. About three months after the onset of her trouble she noticed her hair, which was dark brown, beginning to turn gray and her skin changed to a light bronze color. The hair in the axilla and the pubic hair also began to drop out about the time the

skin began to bronze. Prior to admission to the hospital the patient complained principally of weakness, physical and mental, anorexia, and nausea, with occasional attacks of vomiting.

**Condition on Admission.**—Patient shows evidence of considerable emaciation with a bronze colored skin, with areas of leukoderma about the left ear, on the upper part of the left thorax, and several patches on anterior abdominal wall.

**Physical Examination.**—*Head.*—Hair gray, with evidence of alopecia.

*Eyes.*—No evidence of jaundice of the sclera. Pupils widely dilated and react sluggishly to light and accommodation.

*Mouth.*—Teeth and tonsils negative. Tongue clean and moist. No pigmentation of mucous membrane of the mouth.

*Neck.*—Thyroid glands slightly enlarged.

*Thorax.*—Expansion equal.

*Lungs.*—Clear and resonant throughout, no râles heard.

*Heart.*—Area of cardiac dulness normal, sounds feeble and distant, a soft systolic murmur heard at the apex.

*Abdomen.*—Scaphoid: no areas of tenderness or masses palpable. Liver, spleen, and kidneys not palpable.

*Extremities.*—No edema; reflexes normal.

*Skin.*—Aside from pigmentation, imparts to the touch a sensation of subnormal temperature, is soft, smooth, and elastic.

**Urine examination** on five different occasions negative.

**Wassermann Test.**—Negative.

**Blood Examinations.**—Hb., 93 per cent.; R. B. C., 4,660,000; W. B. C., 15,200; C. I., 1.

Polynuclears, 71 per cent.; eosinophils, 1 per cent.; small mononuclears, 26 per cent.; large mononuclears, 2 per cent. No change of size or staining of red blood-cells.

***x*-Ray examination** of chest negative.

**Tuberculin Test.**—Von Pirquet, negative.

Patient was admitted to the hospital on August 6th and has been so weak that she has not been able to sit up in bed. She attempted to do so once and fainted. During her hospital residence her temperature ranged from 98.6° to 96° F. and her pulse-rate from 100 to 62 per minute; the systolic pressure

varied from 85 to 90 mm. Hg., and diastolic pressure from 60 to 72 mm. Hg., and the respirations were 24 per minute.

Treatment, besides symptomatic, consisted of the use of desiccated extract of suprarenal gland, 6 grains three times daily.

During the hospital stay the patient has been complaining of being cold, and on touching her body in any part the skin is as cold as that of a corpse. Hiccup has been common and nausea frequent, and great persuasion was necessary to get the patient to take food.

The patient stated that prior to the present illness her health had been excellent. This acute illness unquestionably was the beginning of the present condition, although in Addison's disease, as a rule, the onset is insiduous. When the patient was first seen in the hospital her principal complaint was weakness. The pigmentation did not seem to her to be of a great deal of importance. She stated that her mother had areas of pigmentation which were similarly distributed over the body and had been present as long as could be remembered. She was therefore not greatly concerned about any pigmentation present on herself.

The patient's clinical picture was almost typical of Addison's disease, and with the symptoms present at the time she came under observation pointed to the diagnosis with but little difficulty. The general pigmentation of the face contrasted to the pearly conjunctivæ and white teeth, presented a picture not unlike that of a native Philippino.

Although death was not unexpected, it came very suddenly. During the four days previous to the end the patient stated she had "sinking spells," as she termed them, lasting four or five minutes, several times a day, during which she felt very weak and her pulse was almost imperceptible. Nausea was continuous and retching was a most distressing symptom, which yielded to no treatment. The patient took very little food or water for one week prior to her death on account of retching and nausea. Death came during a sleep. It is not uncommon to have the fatal issue take place during sleep or during a syncopal attack.

The different forms of treatment that have been beneficial are the administration of desiccated suprarenal gland, 2 to 5

grains three times daily, or increasing doses of adrenalin given hypodermically. Thymus extract has been given advantageously in connection with the suprarenal products. Stimulants are usually without effect. The nausea, without any apparent cause, is a troublesome problem, and is only occasionally relieved by the usual therapeutic measures. There is no known specific. The use of the glandular extracts has not met with the success which, at first thought, it might be reasonable to expect. One tries suprarenal gland in all cases, but with a doubtful benefit.

The important points taken from the autopsy report, at which the clinical diagnosis of Addison's disease was verified, are as follows:

The mesenteric nodes are enlarged, firm, and yellowish. The heart muscle flabby and shows gross evidence of myocardiac degeneration. The lungs showed no gross evidence of tuberculosis.

No gross evidence of any suprarenal tissue was found, but the fatty tissue in its locality was taken for microscopic examination, with the following report: The suprarenal structure showed a marked connective tissue increase. There was very little cortical tissue, and this in a marked state of degeneration. At the extreme tip of the suprarenals the cortex is thickened and appears to compress the medulla, and probably represents the fibroblastic period of connective tissue formation. The thyroid gland showed a chronic interstitial hyperplasia.

## CLINIC OF DR. T. GRIER MILLER

UNIVERSITY HOSPITAL

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# CARCINOMA OF THE ESOPHAGUS

**Presentation of 2 Cases with Pulmonary Complications, and a Brief Analysis of a Series of 29 Cases.**

I WISH to present the records of 2 patients who have died on the medical service of the University Hospital within the present year of carcinoma of the esophagus and who showed certain unusual features, and consequent difficulties in diagnosis, that were proved at autopsy to have been due to perforations into the pulmonary tissues. In the discussion of these reference will be made to the 29 cases of esophageal malignancy that have been studied on the service during the past fourteen years.

### CASE I

W. O., aged fifty-four, white, male, a native of Germany, was first admitted October 20, 1919, on account of pain in the epigastrium and back. Late in the previous July, immediately after drinking a glass of ice-cold milk, he had been seized with a sharp stabbing pain in the region of the ninth to eleventh thoracic vertebræ. Leaning well forward gave some relief, and in about a minute the pain had entirely passed away. A similar but less severe attack of pain occurred a few weeks later, again coming on immediately after swallowing some food; and in the subsequent month he had several such attacks each day. Then he began to have associated pains in the epigastrium, at first developing about three hours after meals, and being relieved by eating, and later becoming constant and being made worse by pressure. He stated that the pains were much more violent over the week ends. Belching gave some relief; there was no

vomiting. He had had a fairly good appetite up to five weeks before his admission to the hospital, but it was poor thereafter, partly, he thought, because his doctor had put him upon a very light and somewhat monotonous diet. His bowels were regular. He had lost 20 pounds in the six weeks before his coming into our hands. During that time he had developed much weakness and tiredness, although he had been able to keep at his job as janitor in one of the University buildings.

His past medical history was unimportant. He was married, but had no children; otherwise the family history was negative. Previous to taking up the job as janitor at the University five years ago he had been a steward aboard steamers and schooners of various steamship lines. It had always been his habit to take about 2 glasses of whisky and some beer daily.[1]

Physical examination showed evidence of loss of weight in both the panniculus adiposus and in the muscle tissue. His weight was $113\frac{1}{2}$ pounds. The skin had a subicteric hue, was dry, and showed copper-colored spots over the thorax and back. There was a generalized adenopathy and the peripheral blood-vessels were definitely sclerosed, the temporal and brachial vessels especially being noted as tortuous, pulsating, and hardened, and the eye-grounds showed a high degree of arterial sclerosis. The teeth were in bad condition and there was much pyorrhea. The left shoulder was higher than the right. Lungs were negative. The heart was widened to the left, this base measuring 13.5 cm. The apex-beat was forcible and palpable, best felt in the sixth interspace. There was a reduplication of the first sound, but there were no murmurs, and the basal second sounds were accentuated. The abdomen was negative except that the liver edge was palpable and the lower abdominal veins were prominent. The blood-pressure was 154–78.[2]

The intern's tentative diagnosis, made at this time, was advanced general arteriosclerosis.[3]

[1] This history, as is customary on this service, was taken by one of the fourth year medical students acting as a clinical clerk in the medical wards.

[2] This physical examination was made by the intern.

[3] It is the custom for the intern to make and record on the history a tentative diagnosis as soon as his examination is completed.

The routine clinical examinations were made and reported upon as follows:

**Blood.**—4,050,000 red cells; 13,800 white cells; hemoglobin 60 per cent. The differential count revealed 65 per cent. neutrophils, 20 lymphocytes, 11 large mononuclears, 2 transitionals, 1 eosinophil, and 1 basophil.

**Urine.**—Specific gravity varied from 1.009 to 1.027, contained no albumin or casts, and no red blood-cells or excess of leukocytes.

**Phenolsulphonephthalein Test.**—70 per cent. elimination in two hours—60 per cent. in the first hour and 10 per cent. in the second.

**Blood Wassermann.**—Negative.

**Gastric Analysis.**—The contents, obtained forty-five minutes after an Ewald meal, measured 90 c.c. and had a free acidity of 32, with a total acidity of 48. There was no occult blood. There was no difficulty in passing the gastric tube.

**Special eye examination** by Dr. B. F. Baer, Jr.: "O. D. and O. S. show advanced retinal vessel sclerosis."

**Blood-serum** examined for bile—none found.

**A Roentgen examination** of the gastro-intestinal tract showed a constriction of the lower 6 cm. of the esophagus, which was interpreted as being due to cardiospasm. The position of the stomach was normal and there was a continuous moderate hyperperistalsis with an associated commensurate hypermotility. The waves reached the pylorus without interference and there were no defects in the outline of the stomach or duodenal cap. The plates showed nothing further except that they confirmed the finding of a large or low liver. Subsequent roentgenographic study showed a ptosis of both flexures of the colon and very marked colonic stasis.

A second gastric analysis showed no retention, a total acidity of 31, free hydrochloric acid of 12, and occult blood positive.

On November 1st the patient became dissatisfied and demanded his release from the hospital. We were at a loss to know what diagnosis to enter on his record. During his stay three diagnoses had been under consideration, the first one, of arteriosclerosis, having been made by the intern at the time of his original

physical examination, and the others, of hepatic cirrhosis and of cancer of the alimentary tract (location doubtful), having been suggested tentatively and respectively by the two assistants on the ward. The presence of arteriosclerosis was unquestionable, but it did not seem sufficient to explain, as one of the assistants noted at the time, "the steady rapid progress of the symptoms, the loss of weight and weakness, and the patient's appearance." Furthermore, in view of the ease with which the gastric tube passed through the esophagus, the gastric analysis, the negative rectal examination, and the roentgenographic study, the diagnosis of alimentary cancer did not seem justifiable. The apparent hepatic enlargement and the dilated abdominal veins, together with a history of alcoholism, were, however, somewhat suggestive of an early stage of portal cirrhosis, and it occurred to us that the Roentgen finding of constriction in the lower esophagus might have been due to dilated esophageal veins from portal obstruction. We therefore entered a diagnosis of early hepatic cirrhosis, fully realizing at the time that this was not firmly established.

The patient did not improve, and returned to the hospital just one month later. During that time he had been able to do light work for two hours each day, but was so weak that he had to spend the remainder of the day in bed. Until November 26th he had been able to swallow only liquid foods, and on that date he had the sensation, as he said, "as though a trap-door had shut down" in his stomach, stopping the passage of food. Thereafter he had regurgitated liquids just as he had swallowed them. On the day of this second admission (December 1st) he complained of almost constant substernal pain, from the suprasternal notch to the xiphoid, and described it as being "deep inside." Otherwise his symptoms were as on the previous admission.

At this time his weight had dropped to 102 pounds. He was beginning to look quite cachectic, abdomen was scaphoid, the abdominal veins were all the more prominent and the liver edge was not certainly palpable, but a mass was felt and taken to be the right kidney. There were 4,840,000 red blood-cells with a

hemoglobin of 78 per cent. and there was a leukocytosis of 11,400. On December 3d he was able to swallow a little milk, and a roentgenoscopic examination showed that a bismuth meal passed with difficulty through the cardia into the stomach. On the following day Dr. George P. Muller, by an esophagoscopy, discovered a constriction 5 inches below the pharynx, which could, however, be passed by the instrument. After this examination the patient felt much relieved, was able to eat semisolid food, and was convinced in his own mind that the obstruction had been removed. Again he insisted upon leaving the hospital, and went out, against advice, on December 6th.

Four days later he was admitted for the third time on account of a recurrence of the esophageal obstructive symptoms. He was given benzyl benzoate, 7 c.c., five times a day, but without relief of symptoms, and two days later an esophageal bougie was passed; this affording marked relief and permitting him to eat such things as toast, egg, etc., for a few days. Then, in order to minimize the irritation of the suspected esophageal lesion and at the same time to push feeding, a gastric tube of the Einhorn variety was introduced into the stomach, and through this he was given daily food with a value of 1500 to 2000 calories for three days. His general condition improved, and again he was able, without difficulty, to take semisolid food.

On December 21st it was suggested that, on account of the extent of the heart to the left (14 cm. measured on the skin surface), without any other evidence of cardiac pathology and with no heart sounds over the sternal area or to the right of it, where the dulness extended for 4 cm., there might be a mediastinal lesion pushing the heart to the left and producing the esophageal obstruction. A stereoscopic Roentgen examination, however, suggested that the heart itself was enlarged and that there was no mediastinal mass displacing it. The Roentgen report by Dr. H. K. Pancoast, however, read: "Very decided enlargement of the hilus shadow on the right side, cause not determined."

On January 1, 1920 the daily note read: "Patient complains of not being able to take any semisolid food, says his spasm is getting worse." The next day he could not get liquids through.

A bougie was passed and again gave relief. On the 3d he had 21,500 leukocytes, but temperature was normal; red cells numbered 4,210,000 and hemoglobin was 72 per cent. The leukocytes had mounted to 24,700 by the 6th, still there was no fever, and no cause could be discovered for the leukocytosis. From the 8th to the 12th he had a slightly elevated irregular temperature (99° to 100⅖° F.); on the latter date the white blood-cells numbered only 8900. For the next ten days he had a low, irregular fever, but was gaining weight and eating well. On the 22d it was noted that the tongue was red and patchy and that there was a whitish membrane on the buccal mucous membrane, and much pus about the teeth. A smear of the pus showed the fusiform bacilli and spirilla of Vincent. Blood now showed 3,850,000 red cells, 12,400 leukocytes, and 57 per cent. hemoglobin. Sputum showed Type IV pneumococci. Blood urea nitrogen was 19 mg. per 100 c.c. of blood. Fractional gastric analysis showed a free acidity of 10 to 15, with a total acidity of 20 to 30; occult blood was strongly positive. A diagnosis of Vincent's infection was made.

At this time, because of the Roentgen finding at the right pulmonary base and the subsequent clinical course, a neoplasm of the lung was suspected, and a repetition of the stereoroentgenographic study of the chest suggested. This, made on the 26th, showed no change. Three days later, however, a roentgenogram of the esophagus, made after swallowing a bismuth mixture, showed a tight constriction with irregular outline strongly suggesting malignancy.

On February 3d the temperature, which had been normal for a week, began to rise, getting to 102° F. in the course of twenty-four hours, and it continued irregularly until death, on the 8th. This was attributed at the time to a recrudescence of the Vincent infection, many small patches reappearing in the mouth.

On the day of death, without warning, the patient suddenly collapsed, complaining only of vertigo, and soon presented a feeble pulse and moisture in the lungs, death supervening after a few hours.

**Autopsy Findings.**—A complete autopsy was performed by Dr. Baldwin Lucke, who reported upon the esophagus as follows: "In the lower part of the esophagus is a necrotic, gangrenous, fungoid mass which almost occludes the lumen of the organ; this mass has infiltrated and destroyed the entire esophageal wall, and is adherent to the neighboring structures, especially the basal lobe of the left lung, into the substance of which the necrotizing tumor has spread." In describing the gross left lung findings he stated: "Adherent to the basal lobe is a necrotic mass springing from the esophagus, and in the substance of the lobe a ragged walled cavity, an abscess, the size of a fist, containing very foul-smelling brownish fluid. The cavity is near the apex of the heart, and in places almost reaches to the pulmonary surface, separated only by a very thin strip of lung tissue." The rest of the basal lobe he found to contain numerous grayish and reddish-brown consolidated areas; the intervening tissue was very moist and congested. The right lung was moist and bloody, but air containing throughout. The peribronchial lymph-nodes were enlarged, juicy, and congested.

Surrounding the cardiac end of the stomach was found a chain of large, rather firm lymph-glands, about a dozen in number, and averaging from 2 to 4 cm. in diameter. Except at the cardia the stomach was nowhere infiltrated by the esophageal tumor mass. The liver was enlarged, had a dusky red color, and indistinct lobulations. The aorta showed early atheroma.

The microscopic examination proved the tumor to be a very necrotic epithelioma. The lung tissue in the immediate neighborhood was frankly gangrenous; the scattered consolidations were of the type seen in septic lobular pneumonia.

**Discussion of Case I.**—This case is interesting because of the misleading nature of the early symptoms and signs, and the consequent extreme difficulty experienced in arriving at the correct diagnosis. The patient was in the hospital off and on for three and a half months, and although a low esophageal obstruction was indicated by the first roentgenographic study, and it was confirmed by esophagoscopic examination during his

second admission, it was not until the roentgenologist reported a distinct irregularity in the lesion, just ten days before death, that we were convinced of the true nature of the process. In the first instance we were thrown off the proper line of thought by the absence of the usual early symptoms, of dysphagia and localized pain, and by the presence of signs suggestive of liver disease; later, by the absence of anything more definite in the report upon the esophagoscopic study than a constriction and by signs suggesting that this might be due to pressure from without; and finally, by the readiness with which the patient's late dysphagia was overcome by the passage of bougies.

The pulmonary lesions were not diagnosed during life, and here again our failure lay in that our attention was misdirected. When the patient developed a temperature that might ordinarily have caused one to think of a secondary pulmonary condition we found a Vincent's infection of the mouth. Furthermore, the physical signs in the chest were never suggestive, the roentgenograms of the lungs were largely negative (due to the location of the abscess behind the heart), and the patient did not have a cough and expectoration. The latter can be understood when it is pointed out that the gangrenous abscess was low in the chest, probably did not communicate with a bronchus, and almost certainly discharged its contents by way of the esophagus into the stomach.

### CASE II

R. D., aged sixty-four, Irish, white male, was referred from the medical dispensary to the medical wards of the hospital on October 18, 1920.

**Chief Complaint.**—Cough, sleeplessness, and poor appetite.

**Present Illness.**—Following an attack of influenza in February, 1920, he had a gradually increasing but largely nonproductive cough, and for two weeks there had been some anorexia, dyspnea, and sleeplessness. There had been no bloody expectoration. He gave no other history of gastro-intestinal or circulatory disturbance. There were no urinary symptoms.

He had lost about 5 pounds in the three weeks preceding admission.

**Past Medical History.**—He had had only whooping-cough in childhood, spinal meningitis at the age of twenty-nine, and influenza on two occasions, in 1918 and in February, 1920. He denied venereal infection.

**Family History.**—Negative except that his wife had suffered from melancholia since her menopause, and that they had lost 3 children—1 at birth, 1 of an accident, and 1 of pulmonary tuberculosis; 4 children were living and well.

**Social History.**—He had worked in a roller-bearing plant, but was never exposed to an excessive quantity of dust, and the work was not particularly heavy. He lived under good hygienic conditions. Formerly he had used alcohol somewhat excessively; smoked to some extent.

**Physical Examination.**—This examination, as made by the medical intern at the time of admission, was recorded in brief as follows: Patient is a lean, cadaverous, weary looking, white adult male. There is evidence of emaciation, the skin hanging about him very loosely. The skin has a dusky cyanotic tinge, and his scleræ are subicteroid. Mentality is clear. His breath is very foul and during heavy coughing spells he becomes quite dyspneic. His pupils are small and the irides react sluggishly to light, and apparently not at all to accommodation. Tongue is heavily coated and is tremulous. Teeth are in frightful condition, all being mere stumps, and there are pyorrhea and gingivitis. Tonsils and oropharynx are congested.

The chest is rather emphysematous in shape and the supra- and infraclavicular fossæ are prominent. There is some lagging of the left side during inspiration. Movement of the left diaphragm on the chest wall posteriorly cannot be determined. Costal margins move outwardly very slightly during inspiration. The ribs and interspaces are prominent. There is some impairment to percussion over the left chest posteriorly, less marked about the root of the left lung than elsewhere. A few coarse râles are heard over the chest generally, especially over the left chest posteriorly.

The heart outline gives the following measurements: right base 2 cm., left base $10\frac{1}{2}$ cm., right oblique $9\frac{1}{2}$ cm., left oblique 14 cm., and height 12 cm. The apex-beat is not visible and only vaguely palpable. There are no murmurs, arhythmias, or impairment of muscle sounds. The pulmonic second sound is accentuated. Abdomen and genitalia are normal. Rectal examination is negative. The deep and superficial reflexes are normal. There is cyanosis and beginning clubbing of the fingers. The radial and brachial arteries show evidence of sclerosis.

The intern's preliminary tentative diagnosis, based upon the history and his physical examination alone, was "bronchiectatic cavities in left lung."

Subsequently the following clinical examinations were made and reported upon:

(1) *Urine.*—Negative but for a very faint trace of albumin and some hyaline, light and dark granular casts.

(2) *Blood.*—Red cells 3,480,000; leukocytes 13,300; hemoglobin 71 per cent.; differential, normal.

(3) *Sputum.*—Seropurulent, greenish, of necrotic odor, no elastic fibers or tubercle bacilli; culture showed Gram-negative rods and non-hemolytic streptococci.

(4) *Phenolsulphonephthalein Test.*—30 per cent. elimination in the first hour, subsequent collections not reported upon.

(5) *Blood Wassermann.*—Negative.

(6) *Blood-pressure.*—115 systolic, 65 diastolic.

(7) *Laryngeal Examination.*—Slight infiltration of the left arytenoid cartilage, which was regarded as somewhat suspicious of tuberculosis.

On October 21st one of the assistants on the service made a note calling attention to the harassing, brassy, usually unproductive cough and the extremely foul odor of the breath. He also noted a supracardiac area of dulness, measuring 10 cm. in width, in both the first and second interspaces. The heart he found wider than previously recorded, 12 cm. to the left and 4 cm. to the right of the midline, and there was a faint systolic murmur at the aortic area. At the left pulmonary apex posteriorly was found distinct impairment on percussion and there

were a few râles. At the left base were found slight impairment on percussion and a few dry and moist râles. On the basis of the data accumulated at this time the following diagnostic suggestions were noted: "An old tuberculous lesion at the left apex; mediastinal involvement, tuberculous or aneurysmal; bronchitis with probably small bronchiectatic cavities at the left base."

The following day a Roentgen study of the chest was reported upon as follows: "There is a lesion at each base with marked fibrosis, significance uncertain."

On the 23d examination of the lungs by the intern showed dulness at the left apex, extending down to the angle of the scapula, and the percussion note seemed more impaired at the right base than at the left, but there were still no changes in the auscultatory signs. He added that a diagnosis of bronchopneumonia, superadded to whatever the fundamental pulmonary condition might be, deserved consideration; and for the following reasons:

(1) The sudden increase in symptoms two weeks before, with subsequent increasing dyspnea.

(2) The variability of the chest signs.

(3) The irregular temperature curve (97° to 103° F.) which had been present since admission.

(4) The leukocytosis.

(5) The Roentgen evidence of lesions at the bases.

On the 24th the patient grew weaker gradually, blood-pressure dropped, pulse became intermittent; he complained of severe pain in the precordium, and finally died.

**Autopsy Findings.**—This autopsy also was performed by Dr. Lucke. He found the lower fourth of the upper lobe and most of the basal lobe of the left lung almost solid. The cut surface of these areas showed many grayish-yellow spots of consolidation, tending toward confluency. In the right lung the basal lobe contained many firm areas and in the upper lobe were scattered firm areas. The peribronchial lymph-glands were markedly enlarged and juicy.

At the point in the trachea where the right bronchus normally comes off was an area of complete erosion (2 x 3 cm.) which led

into a sac-like cavity, $5\frac{1}{2}$ cm. in depth and $2\frac{1}{2}$ cm. in width, the interior wall being ragged and containing foul-smelling material. At the lower end of the cavity the remaining portion of the right bronchus was recognized, indicating that the cavity represented a complete erosion of the first portion of this bronchus and a dilatation of the reparative fibrous wall. What appeared to be a very large caseous lymph-node lay against the wall of the cavity, but upon dissection it was found that this was really a

Fig. 128.—Specimen from Case II. The pale mass in the opened esophagus is the epithelioma. The ragged opening in the trachea is shown between the two glass rods. (Courtesy of Dr. Baldwin Lucke.)

tumor of the esophagus. When the latter was opened a pale white, somewhat firm, and partly necrotic mass was seen to obstruct almost the entire lumen. This tumor lay behind the bifurcation of the trachea, was nodular, and formed an irregular ring. No distinct communication could be traced between the cancer and the erosion of the right bronchus, but because of the evidently newly formed connective tissue walling off the eroded portion Dr. Lucke felt that such a connection had existed

at one time. Microscopic study showed the tumor to be a partly necrotic epithelioma.

**Discussion of Case II.**—The bronchopneumonia above described was, of course, properly identified clinically on October 23d, five days after the patient's admission, but the finding of an esophageal carcinoma at necropsy was surprising. This caused a careful review of the case record to determine whether or not any possible clue had been overlooked. The history as obtained in the ward was certainly not in the least suggestive, but in going further back into the dispensary records, which had not been seen up to this time, it was found that the historian had obtained a statement from the patient to the effect that he had been obliged to wash down his solid food with water. This item of history was of the greatest importance and was a clue that would almost certainly have led to a diagnosis had it been appreciated in the wards. Because of the failure to elicit this history in the wards and because of the patient's ability to take without complaint the soft diet which was ordered for him, no attempt had been made to pass a stomach-tube or a bougie, to esophagoscope him, to look for blood in his stools, or to make a Roentgen study of the gastro-intestinal tract. His physical condition would perhaps in any case have rendered inadvisable the introduction of instruments into his esophagus, but a roentgenographic study was certainly possible, and this alone would probably have made the diagnosis. Thus this case particularly emphasizes the extreme diagnostic value of careful and exhaustive history taking.

**General Discussion.**—The postmortem examinations on these 2 cases revealed errors in diagnosis that are perhaps more commonly made than is generally appreciated. In the one the primary disease was finally recognized clinically, but not the complication, while in the other the secondary process, but not the original affection, was diagnosed. The latter is perhaps the less likely mistake, but, as our case shows, it is a possibility. The former is undoubtedly a frequent error, as statistics from the autopsy table show that perforation of the esophagus occurs in about one-half of all cancer cases, while clinically they are recog-

nized only occasionally. It is usually assumed that when the air tracts are perforated the swallowing of food sets up a cough, with often the expectoration of food particles, and that when an opaque meal is swallowed under the roentgenoscope it can be seen entering the air passages, thus making the diagnosis; but, as both our cases show, neither of these things need necessarily occur. In the first instance the bismuth did not enter the pulmonary cavity, probably because the latter was entirely filled with material, and if food did enter the cavity it could not be coughed up because the bronchi were closed off from the diseased area by an inflammatory reaction. In the second case neither of these diagnostic phenomena could occur while the patient was under our observation because by that time the communication between the trachea and the esophagus had become occluded.

Because of such possibilities of error it is well to remember that once the fact of esophageal stenosis is established in a person past middle life, and where there is no apparent cause, cancer is a good surmise. In point of frequency this organ stands fourth among the parts of the body so affected, being exceeded only by the stomach, the uterus, and the breast. It forms 5 to 7 per cent. of all cancer encountered in man. The neoplasms are usually of the soft variety, readily degenerate, and because of irritation from the opposing walls and the passage of food, with the implantation of bacteria, they tend to ulcerate extensively. This process leads to early involvement of adjacent structures, and, because of the importance of the latter, various striking clinical pictures are presented. Unless such pictures, as complications, are kept in mind the original disease may be overlooked.

Perforations, as stated, are not infrequent. They occur most often into the larger air passages: the larynx, trachea, and bronchi; but also into the mediastinum, pleura, lung, aorta, and pericardium. Such perforations into the air passages are not immediately fatal, but they lead to lung infection, with the development of bronchopneumonia, abscess, or gangrene, these conditions determining the fatal outcome. When the medias-

tinum is involved an infective interstitial emphysema of the neck tissues occurs. In other instances perforation may lead to immediate death, as when the aorta or other large blood-vessel is involved, the complication being appreciated clinically by hemorrhage from the mouth.

Aside from these perforations, the growth may involve such other structures in intimate relation with it as the left recurrent laryngeal nerve, giving laryngeal paralysis, and cases have been reported in which the vertebræ were involved, and even the spinal cord itself, with a consequent paraphlegia. Secondary deposits often occur in the cervical and mediastinal glands, and in the glands about the cardia of the stomach, and also in the stomach wall itself, the diaphragm, the liver, and the peritoneum.

### ANALYSIS OF DATA ON 29 CASES

Perhaps I can now best present the usual picture seen in patients suffering from cancer of the esophagus by analyzing briefly such data as we have on the 29 cases that have been studied on the service of Dr. Alfred Stengel since January, 1907. They were distributed, according to years, as follows: 1 case each in 1909, 1910, 1911, and 1918; 2 in 1907, 1909, 1914, 1915, and 1917; 3 in 1912, 1916, and 1919; and 6 thus far in 1920. There is no obvious explanation for the increase during the present year, the number of beds not having been increased during the past decade.

The ages of the patients varied from forty-one to eighty-two, with an average of fifty-seven and nine-tenths and a median of fifty-six. This is in accordance with the available published statistics. Males predominated in the proportion of about 5 to 1, there being 24 males and 5 females, a female percentage of 17.2. This is a higher female ratio than is generally accepted. All were Caucasian, the Americans, Irish, and Germans predominating, with the following respective figures: 9, 6, and 5. These figures, however, are not significant, since they represent roughly the percentages of these nationalities in our wards. No special occupation was favored, no more than two having the same, these being farmers, gardeners, and machinists. It is recognized that alcoholism is frequently associated with this

disease, and to this our series lends support. Seven stated that they were excessive users of alcohol, 9 moderate users, and 5 drank to some extent. In only 5 instances was a negative history obtained, and these were all women. The Wassermann test was done in 19 instances and in 18 it was negative; in the other 1, proved at operation to be malignant, it was moderately positive. Of the 10 patients in whom no test was recorded, 3 denied luetic infection, and there was no suggestive history in any of them.

The duration of symptoms before admission to the hospital varied from three weeks to fifteen months, with an average of six months. In every instance there was obtained a statement which suggested some difficulty in swallowing, in the beginning usually of solid foods only, but often of both solids and liquids. Sometimes the food would pass through, but the patient was aware of some discomfort, usually referred to the xiphoid area, and often spoke of a sense of obstruction; in an even greater number of instances he told of an actual regurgitation of food soon after swallowing it. When pain was present its location was of interest. In our series it was localized in the lower sternal area 11 times; in the epigastrium, 8 times; the back, 5 times; the shoulders, 3 times, and in the upper sternal region twice. The reference to the back is of importance in connection with our first case, W. O., who had as his initial symptom sudden severe pain in the lower thoracic spinal region, and this associated with the swallowing of a cold liquid at that instant is significant diagnostically. It recalls the experimental work of Hertz,[1] who found that the sudden inflation of a balloon in the esophagus gave rise to a sensation of pain accurately localized deep in front and associated invariably with pain at exactly the same level behind. So long as the sensation was only that of fulness or obstruction it was never referred to the back. He believed this to be a true referred pain, "the afferent impulses from the esophagus in these cases being conveyed by sympathetic fibers to the segment of the spinal cord, which supplies the sen-

[1] Hertz, Arthur F.: The Sensibility of the Alimentary Canal, Oxford University Press, 1911, p. 52.

sory nerves to the muscular and other tissues, in which the referred pain is felt." In this connection also another of our cases was interesting in that there was a complaint of pain in the left face. This reference of pain is probably similar to that of brow-ache from swallowing ice-cream, which Hertz explains as being due to sensory impulses passing up the vagus and "increasing the irritability of a part of the neighboring nucleus of the fifth nerve." The other significant item of history related to weight loss, which was mentioned in almost every instance and ranged as high as 80 pounds, usually 30 to 40.

In spite of this rather marked loss in weight, which was probably largely due to insufficient intake of food, the blood-picture was not markedly affected, the average hemoglobin reading being 68 per cent., and the average red cell count 4,240,000. In only 6 patients was the initial hemoglobin reading less than 60 per cent. The leukocytes numbered from 5800 to 22,800, but, with a single exception, were 15,000 or less, the majority being within normal limits.

The site of the lesion in the esophagus, as determined by the distance a tube could be passed, by esophagoscopy, by roentgenoscopic study, or by necropsy, or by a combination of these methods, was as follows: 2 of the tumors were situated in the cervical portion of the esophagus, while 8 were in the upper thoracic portion (beginning at the bifurcation of the trachea), and 19 were in the lower third.

Of the 29 patients, 22 were roentgenographically studied and 11 had one or more esophagoscopies; 9 required gastrostomies while in the hospital, and 5 of these died within a few days afterward; 3 were treated with radium, but none was apparently benefited, although recent experience in the Roentgen laboratory of this hospital suggests that such treatment, if begun early, prolongs life, gives decided comfort, and often obviates the necessity of a gastrostomy.

There were 8 deaths in the hospital, but only 3 autopsies were obtained. Two of these necropsies are reported above, each showing a perforation, while the third one, on the body of a patient who had had a gastrostomy performed three weeks

before and had been treated with radium for several months, showed an almost completely occluded esophagus, but no perforation, and metastasis only to some neighboring lymph-glands. There was clinical evidence of metastasis to the right supraclavicular glands in one case, to the stomach in one operative case, and to the liver in another. It is reasonable to suppose that most of the others had metastases of some kind, and that perforations were present in some of them.

## CLINIC OF DR. JOSEPH C. DOANE

PHILADELPHIA GENERAL HOSPITAL

### SOME MANIFESTATIONS OF ALCOHOLISM

To the minds of many, alcoholic inebriety suggests but the vision of a reeling figure, reeking with the fumes of a liquor, the character of which depends on the purse and the prominence of the individual. To the initiated, the picture above suggested is but the commonest, and least interesting, of the many and varied clinical manifestations produced by alcohol in toxic doses. It is the purpose of this clinic to illustrate a few of the mental and physical states by which the physician is frequently confronted, and to suggest very briefly some fundamental points in diagnosis and treatment; for, in spite of legal enactment, it seems likely that for some time to come the physician must needs meet the problems incident to the toxic effect of alcohol. Especially today must we be alert to detect not only this easily recognizable and still not infrequent classical picture of acute inebriety, but also the less common, and often undetected symptomatology, due to the many alcohol-containing preparations, with more or less harmful drugs in combination.

Not a few deaths have resulted in the past year from the imbibition of various pharmaceutic preparations containing methyl alcohol. The prostration, the violent gastro-intestinal reaction, the visual disturbances, and frequently the history of the consumption of an unknown preparation, or one known to contain wood alcohol, usually suffices to put us on our guard. We have seen but a comparatively few such cases in the past few months, but while the public is more aware than formerly of the existence of an alcohol quickly death dealing in its effect, a considerable number of cases may arise at any time as a result of a convivial company, all partaking of the same preparation.

It is of interest to note that in this hospital while in 1919, 1471 patients suffering from acute alcoholic inebriety were admitted, in 1920 there were 807 such cases—evidence enough of the difficulties encountered when men endeavor by legislation to uproot an impulse, frequently so complex and little understood in its causation. Just as chemically there is a striking similarity between alcohol and ether, so do we find that the reaction of the central nervous system to the effect of these drugs is in many ways identical. The therapeutic effects of alcohol, ether, and opium on the brain and cord differ mainly in rapidity and permanency of action, and death from either one is caused by a toxic depression of the higher centers.

Alcohol, then, may be classed as a narcotic, and as such finds its proper place in any adequate discussion of the drug intoxications. Not only should mention be made of its toxic mental and nervous changes, but, being a direct protoplasmic irritant and dehydrator, alcohol, brought in long-continued contact with bodily tissues, leaves in its wake the classical sclerotic changes so well known to the physician. For practical purposes we may classify roughly the cases which find their way to a large municipal hospital into five groups, namely: the mental changes incident to chronic alcoholism; alcoholic delirium, acute; dipsomania; polyneuritic psychoses; and acute alcoholic delusional and confusional states.

This morning we desire to illustrate several of these interesting conditions by means of a few selected cases:

**Case I.**—O. McG., aged forty years, ironworker by occupation, was readmitted on December 5, 1920, after having been out of the hospital but four weeks. On admission the patient was not acutely intoxicated, and, while extremely nervous, was not actively hallucinatory.

The record keeper informs us that this is his forty-seventh admission to this hospital for the treatment of alcoholism.

On October 17, 1920 this patient was brought to the hospital in a state of acute hallucinosis, associated with tremors and a history of prolonged drinking. During his stay on this occasion, after a period of apparent progress toward recovery, on November

2, 1920 he again became noisy and difficult to manage, requiring restraint. Six days later, after being three days out of bed, the patient again became disturbed; the tremors of fingers and tongue returned, but mild sedation prevented another setback. On his last admission there was a similar recurrence, after being normal for several days.

Physical examination reveals, as you see, the typical facies of the chronic alcoholic. The pupils react sluggishly, and fine tremors of the tongue, lips, and fingers are present. There are no other striking physical findings except moderate peripheral arteriosclerosis and a palpable liver.

*Comment.*—This is a case of chronic alcoholism of long standing, and a presumably high tolerance. I have treated this patient for at least four attacks of acute alcoholic delirium, and have aborted as many more by the preventive measures to be discussed in connection with our next case.

The progressive physical and psychical deterioration which accompanies the long-continued use of alcohol frequently goes unnoticed. From a state of apparent hypernutrition to one of cachexia, in which the patient is tremulous, emaciated, incompetent, and incapable, is but a matter of degree, dependent on time and the quantity of alcohol consumed. The psychic changes range from a mere irritability with members of his family over trifling matters to a state of egoism, disinclination to work, loss of will power, and of the ability to concentrate.

This patient as an ironworker could benefit by the unusual opportunities offered skilled labor today—instead he does station porter or hospital orderly work, at a low wage. Instead of his facing the world, and asking or giving no quarter, he slinks from saloon to hospital, and hospital to saloon, only stopping for a few days enroute to replenish his money or his health, so as to be able to spend the more lavishly.

I call your attention to the several recurrences of certain mental and nervous symptoms during treatment on his last two admissions. We have seen this occur in this patient on a number of occasions. At one time, after a satisfactory convalescence from delirium tremens, this patient, after smoking a pipe of strong

tobacco, was found wandering in the yard of the hospital, acutely delirious. This probably accounts for one of the relapses chronicled above.

It appears that after, or during, the recovery from an acute hallucinosis, the nervous and mental balance in some patients is so easily disturbed that the mere addition of a moderate dose of nicotin or of alcohol is sufficient to produce a relapse. We have been able to make similar observations in a number of instances.

The prognosis for permanent relief in this type of alcoholic is of course, most unfavorable; for no treatment, with which we are familiar, can replace or repair diseased and deteriorated moral or mental fiber.

**Case II.**—C. S., aged forty years, a salesman by occupation, was admitted to this hospital on November 30, 1920, in a state of delirium—showing great excitement when reaching the ward. He had definite auditory and visual hallucinations, the latter predominating; consciousness was clouded, and the patient was disoriented as to time, place, and person.

This attack began three days ago, with convulsions, after a prolonged alcoholic debauch. A history of gastric intolerance was not procured. A similar attack occurred one year ago, initiated by convulsive seizures, in which the patient, after a premonitory cry, became rigid, and "shook from head to foot."

Physical examination shows, as you see, an undernourished, poorly developed male, but with no apparent degenerative stigmata, and with normal pupillary reactions. There are visible fine tremors of the tongue, lips, and fingers. The bicipital reflex is active, but the patellar reflex is delayed on both sides. Further examination fails to reveal other than the usual sclerotic and fatty physical changes.

*Comment.*—This patient exhibits in his history several very interesting clinical facts. This attack began with convulsions, closely simulating epilepsy, and yet no history of other such seizures exists, except those of one year ago, following a period of heavy drinking.

When coming under our observation he was apparently in the second, or hallucinatory, stage of alcoholic delirium. We do not frequently see delirium tremens begin in such a stormy manner, and by some writers the term "alcoholic epilepsy" is given to this condition. A few days of gastric irritability and intolerance, a developing tremor of the fingers and tongue, and, of greatest importance, a fear to close the eyes as night approaches, are the usual premonitory signs. Then follows the stage in which we first saw our patient—of active hallucinosis.

It is most important to realize that the symptomatology is so divided, for herein lies much of the success of preventive treatment. The visual hallucinosis does not often take the form of the patient trying to evade serpents which are about his bed—the general lay belief of this complication of chronic alcoholism being erroneous in this respect.

Let us remind you that alcoholic delirium occurs in the chronic alcoholic who has gained a high tolerance for the drug; that the type of inebriate who drinks to excess only at intervals, and who has no such tolerance, rarely, if ever, develops alcoholic delirium. It is also to be remembered that a patient who exhibits maniacal tendencies, but who quickly returns to normal under eliminative treatment, usually possesses a low tolerance, and develops not a true delirium tremens, but an alcoholic mania. The differential diagnosis is of importance, and is usually easily made. The former is distinguished from the latter by the tremor, the slower onset, the intense fears, as contrasted with the pugnacious spirit of the latter, and the longer duration of the attack.

The delirium in this patient persisted for seven days, and, as you can see, has now completely disappeared. The pathogenesis of this condition is obscure. Many and varied explanations have been offered, but this seems proved: that the attack is certainly precipitated by a failure to obtain or retain alcohol, which must in turn result in a sudden fall in the amount of circulating alcohol in the vascular and cerebrospinal systems. That there is a lowering in the blood alkali reserve has been proved by Marriott, Hogan, and others, hence the rationale of the exhibition of alkali in large quantities.

As to further treatment, time permits but little to be said. Alcohol administered in the incubation period in quantities sufficient to control the tremor (used merely as an indicator), spinal puncture, hydrotherapy, alkalis by vein (where the stomach is not retentive), and eliminative measures are all useful. Let me warn against the injudicious use of the depressive narcotics, for while the family pride often causes the physician to be urged to quickly quiet the ravings of the unfortunate patient, great damage is frequently done, if, indeed, the massive exhibition of these drugs does not unfavorably terminate the case. The use of mechanical restraint, of the depressant drugs, as well as the general tendency to polypharmacy in the treatment of the alcoholic states, especially alcoholic delirium, cannot be too strongly deprecated. The early routine administration of alcohol to all patients on admission for any cause, who have evidences or history of inebriety, seems but a reasonable precaution. Especially does this seem wise when, from a compilation of mortality statistics, covering the work of many of the best hospitals, we learn that 26 per cent. of patients suffering with delirium, alcoholic, alone or as a complication, die. Realization on the part of the physician that he is dealing with a condition which usually covers a period of from five to seven days, and which cannot be relieved at once by a forced sleep produced by the narcotics, is of prime importance.

One of the most discouraging features encountered in treating these cases is that from the very start we must realize that grave damage has already been done to the cardiovascular system.

Case III.—E. F., aged fifty-four years, laborer, was admitted to this hospital on December 6, 1920, after applying to the police for treatment for rheumatism. While being admitted, although he had been hitherto quiet and rational, the patient suddenly began to scream "murder," and to endeavor to escape. He complained that he heard people saying that he was going to die, and that they repeatedly bade him good-bye.

On admission to the ward he was surly, recognized the doctor as a priest, but denied the use of alcohol.

Physical examination showed equal and promptly reacting pupils to both light and accommodation, and no tremors or speech defect. Auditory hallucinations were still dominant and the peripheral reflexes were normal.

Five days after admission, as his condition had greatly improved, the patient was allowed more freedom. On December 12, 1920 he suddenly attacked an orderly, evidently falsely recognizing in him some person who was about to do him harm. The patient, after having been quieted, spoke of having bought the hospital for $3,000,000, and expressed the opinion that no one had a right to detain him here. While still hallucinatory, a state of depression then followed, during which he was with difficulty persuaded to take food. Perseveration was now present, a stereotyped prayer being repeated for hours at a time. But slight improvement has been noted since admission, for the patient still remains hallucinatory, and with marked delusions of persecution.

The Wassermann reaction is negative in all antigens.

*Comment.*—This is a case of acute hallucinosis, of evident alcoholic origin.

May I invite your attention to several features of this third case, which clearly distinguish this type from the patient just shown. You may have noticed that mention has been made of the predominance of auditory hallucinations, and that there was a distinct persecutory trend to his false beliefs. Then, too, in acute alcoholic hallucinosis consciousness is usually not clouded, and orientation is preserved.

Ward conduct was normal for periods of several days, and when the outbreaks mentioned in his history took place, there were well-founded delusional reasons for his actions. May I also call your attention to the absence of tremors in this patient. Not infrequently the examining physician fails to detect a fine tremor of the tongue, which, when not marked, is best seen along the lateral margin of the tip; as you see, no tremor exists. The duration of this patient's illness also contrasts with the critical termination of that of alcoholic delirium. While many points of variance are discovered in the study of these two alcoholic

states, there is good authority for the belief that they are but a varied manifestation of the same toxic disorder.

Our next patient is one of interest, since the diagnosis for a time was greatly in doubt.

**Case IV.**—F. P., aged thirty-five years, a chef by occupation, was admitted on December 1, 1920, with no history. On admission he was greatly excited, and restraint was necessary. He had visual hallucinations, but heard no voices. There was no disturbance of memory for recent or remote events. Answers to questions were incoherent and unintelligible. Speech was slurring, and strongly suggested the classical paretic type. As you see, even now there is a hesitancy and slurring in his enunciation.

His family history is negative, save for an alcoholic history on the part of his father.

The patient states that he has consumed alcohol to excess frequently, and we may infer that there have not been long periods of sobriety intervening.

Physical examination reveals a well-nourished adult. Pupils were almost rigid in their response to light. There was, and is, a fine tremor of the lips, tongue, and fingers. The examining physician was not able to test the gait and station of this patient on admission. The patellar reflexes are present, but unequal in response time. Examination today shows orientation; no memory defects; no hallucinations or delusions. There is no evidence of neuritis, nor does the patient show any tendency to fabrication.

*Comment.*—A provisional diagnosis of paresis was made on admission, based on the faulty pupillary reaction, the slurring speech, the altered peripheral reflexes, and the general ward conduct of the patient, although later events made a revision of this diagnosis necessary.

Medical literature frequently makes mention of the existence of a condition, in some ways resembling general paralysis in its early stages, to which the term "pseudoparesis alcoholica" has been applied. The neuritic phenomena associated with Korsakoff's syndrome, along with certain mental and physical changes, furnish some symptoms suggesting true paresis.

Although our patient exhibited a striking rigidity of the pupils to light on first examination, today, while sluggish, the reaction to both light and accommodation appears not abnormal.

Neussel, Mignot, Turner, Thomsen, and others have described varying changed reactions to light in the alcoholic pupil, but none of these writers appears to be able to advance any very satisfactory explanation for his findings.

As is well known, hallucinosis, as was seen in this patient, is rather rare in paresis, unless this disease is complicated by alcoholism, uremia, or some other toxic condition. The excitement exhibited on admission is not a rare symptom in the course of general paralysis. But to all of us the slurring speech is frequently one of the early signs which arouse our suspicions of the true nature of the disease. Today we still notice the presence of this symptom, and on questioning our patient we learn that this has existed for many years, and is, in fact, a queer personal habit or inheritance, having no connection, either diagnostically or otherwise, with his present condition. Our provisional diagnosis is further refuted by the Wassermann reaction in both blood and spinal fluid, which is negative in all antigens.

We desire to suggest in this case a diagnosis of acute alcoholic delirium. The interest of this case to us lay in the queer combination of more or less accidental features which made an incorrect provisional diagnosis at the time seem the only logical possibility.

It appears timely to make some mention of the relation of alcoholism and other narcotism, in the light of the recent Federal and State enactments, relative to the non-medicinal use of these drugs.

Many uninformed persons were quick to predict, and later to reaffirm their belief, that in the absence of alcohol there would be a great increase in the illegal consumption of opium and its derivatives.

In the first place, even the casual observer can see the many striking differences between the alcoholic and the so-called drug habitué. The former may be, and frequently is, truthful, honest, able to meet your gaze with ease, capable of conducting

business fairly until the later stages, respects—even in long-standing cases—the decencies, is fond of family and friend, and is loyal to them; the latter usually is essentially untruthful, shifty eyed, neglectful, and unable or unwilling to conduct his business honestly, worships drug above all else, will steal from his family even though his children are in want—in fine, is wholly without healthy moral fiber.

Then, too, there is a common belief among the drug users that if alcohol is used, a supposed combination, extremely deleterious to their health, is formed. The alcoholic feels but scorn for the drug habitué, even though he himself has reached what would appear to be the lowest stages of his vice.

It has been our privilege to question carefully several hundred drug users since July 1, 1919, and we have yet to find a single authenticated case where an inability to get alcohol was responsible for the use of opium or any of its derivatives, nor has it been proved, statistically, that there is any appreciable increase in the total number of opium addicts coming under the observation of the Federal authorities since the enforcement of the 18th Amendment.

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